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American Heart Journal

VOL. 51 FEBRUARY, 1956 No. 2

Original Communications

THE BALLISTOCARDIOGRAPHIC CIGARETTE TEST: FURTHER OBSERVATIONS

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BALTIMORE, MD.

IN A previous communication in this JOURNAL, the effects of smoking on the ballistocardiograms of normal subjects and patients with coronary artery disease were reported.[1] It is the purpose of this report to document subsequent experience with this procedure.

The experience of others was reviewed in the previous report,[1] and will not be repeated here. Henderson,[2] whose observations initially stimulated our interest in this test, has reported his observations in detail. Utilizing the high-frequency bed ballistocardiograph, and observing the effects of smoking one cigarette on ballistocardiographic form and amplitude, he found that in fifty healthy young persons no significant alteration in form occurred after smoking. In thirty subjects from 40 to 60 years of age, a temporary alteration (abnormality) of form appeared with smoking in four instances. In forty patients with clinically evident coronary artery disease, 38 per cent became abnormal or more abnormal after smoking. All of four subjects with diseases frequently complicated by coronary heart disease (idiopathic hypercholesterolemia, Buerger's disease, and diabetes mellitus) showed ballistic abnormality after smoking.

Kelly and associates,[3] testing the thesis that ballistocardiographic deterioration after smoking is due to the presence of disease of the coronary arteries, rather than portal pooling or respiratory effect as they had previously reported,[4]

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*Research Associate, Howard Hughes Medical Foundation.

subjected 100 youths (aged 14 to 18 years), presumably free of significant coronary atherosclerosis, to the ballistocardiographic cigarette test. All subjects had normal control ballistocardiograms. No "real abnormalities" occurred after smoking in this group. Simon and associates[5] performed cigarette tests on fourteen male subjects below the age of 41 years who showed no clinical evidence of heart disease. No significant changes in form or ballistocardiographically determined cardiac output occurred, with either ordinary cigarettes or those of "low nicotine" content smoked through a silica gel filter. Russek and coworkers[6] found ballistocardiographic form deterioration in eighteen of thirty-seven subjects with clinical coronary disease. Buff[7] studied the ballistocardiographic response to smoking of 400 normal persons under the age of 40 years. Ten per cent of the control tracings were abnormal. Of those subjects in the third decade, 5 per cent showed abnormal responses to smoking, while 15 per cent of those between the ages of 30 and 40 responded abnormally.

The present study represents an extension of observations on the cigarette test, with an attempt (1) to report the over-all results of a large number of such tests, (2) to document the findings of multiple tests performed at varying time intervals, and (3) to discuss briefly certain ancillary factors pertaining to this test.

METHODS AND MATERIALS

All subjects were studied on a high-frequency undamped ballistocardiograph in a manner previously described.[8] Twelve lead electrocardiograms were obtained in the usual fashion. A small group of subjects was studied on the aperiodic (mercury) bed.[9]

Selection of subjects was by criteria previously described. This report is limited to individuals meeting our criteria for clinical normalcy[8] and to those having clinically unequivocal angina pectoris or previous myocardial infarction.[10] All other subjects have been carefully excluded from the following tabulations.

The cigarette test was performed in a manner previously described.[1] No effort was made to obtain these observations under basal conditions, but the test was performed after twenty minutes of rest on the ballistocardiograph table. All subjects smoked standard brand cigarettes, inhaling when possible, although many abstained from inhalation. In every case ballistocardiogram, blood pressure, and electrocardiogram were obtained before, immediately after, and five minutes after smoking. In many instances tracings were also obtained thirty seconds and 150 seconds after the institution of smoking. In those tests in which multiple test agents were used, at least ten minutes elapsed after completion of smoking, and a second set of control records was obtained; the next smoking test was then performed in the same manner as the first.

Ballistocardiographic response was classified in the manner previously reported.[1] No significant deterioration of ballistocardiographic form, irrespective of control normality or abnormality, was considered a negative cigarette test. Deterioration of the majority of complexes was classed as a positive response. When deterioration was limited to expiratory complexes only, the result was arbitrarily called borderline. Simple increase in respiratory variation in amplitude was considered a negative response.

Selected tests were performed with filters and with cigarettes of low nicotine content. These were carried out after the standard cigarette test, as described previously.

A total of 252 normal control subjects was studied, and in 102 of these there were repeat tests on at least one occasion, often on several. One hundred ninety patients with coronary artery disease were tested, with fifty-seven tests repeated at least once.

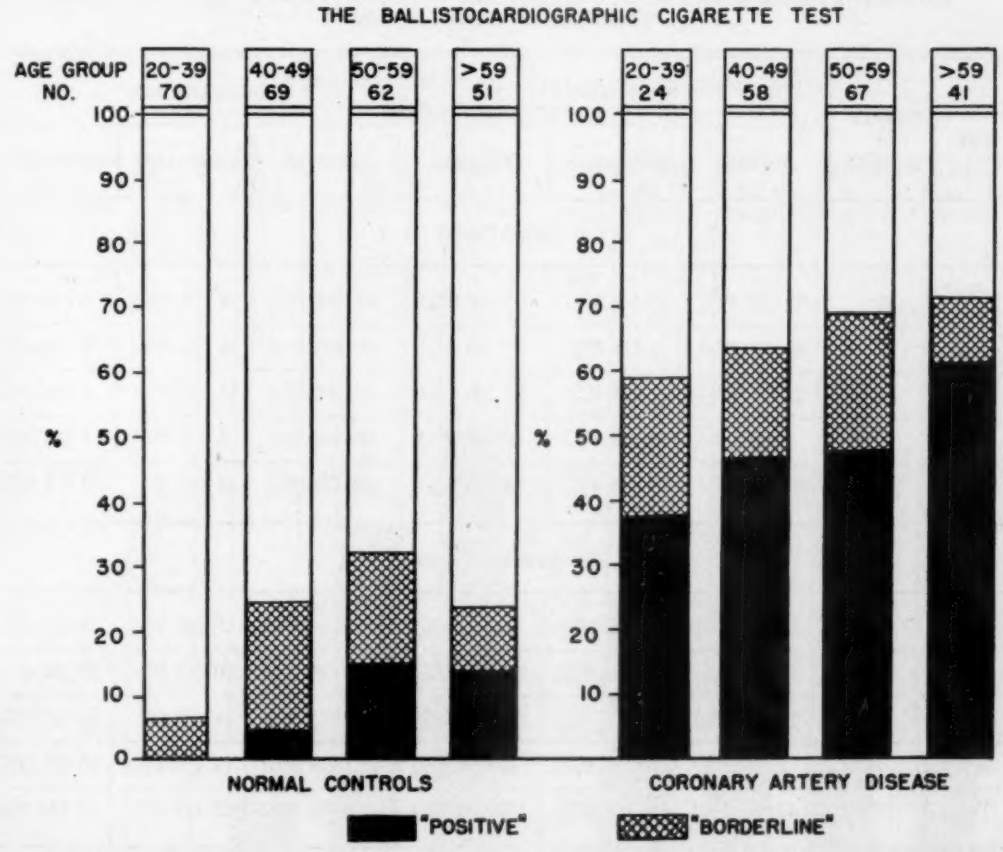

Fig. 1.—The incidence of borderline and positive ballistocardiographic cigarette tests in normal control subjects and patients with coronary artery disease. The columns represent decades (the first column in each representing two decades, the latter three columns in each representing one decade), and the number of subjects in each column is presented at the top of the column. (The differences in incidence of positive tests between normal and diseased groups is statistically significant in each decade.)

RESULTS

Table I summarizes the results of the cigarette test, as well as the incidence of control abnormality by decade and by sex.

The over-all results of the cigarette test are displayed graphically in Fig. 1. In the normal control group, 61.6 per cent had normal control ballistocardiograms, 13.1 per cent had borderline patterns, and 25.3 per cent showed abnormal resting tracings. The ballistocardiographic cigarette test was negative in 199

(79.0 per cent) of 252 subjects. Of the remainder, 13.5 per cent of the responses were considered borderline and 7.5 per cent were considered positive.

Of the patients with clinical coronary artery disease, the resting control ballistocardiogram was normal in 24.7 per cent, borderline in 18.9 per cent, and abnormal in 56.4 per cent. The response to smoking was negative in 33.7 per cent, borderline in 17.4 per cent, and positive in 48.9 per cent.

TABLE I. INCIDENCE OF NORMAL, BORDERLINE, AND ABNORMAL BALLISTOCARDIOGRAMS AND NEGATIVE, BORDERLINE AND POSITIVE BALLISTOCARDIOGRAPHIC CIGARETTE TESTS IN NORMAL CONTROL SUBJECTS AND PATIENTS WITH CORONARY ARTERY DISEASE

AGE	NUMBER OF SUBJECTS	CONTROL BCG			CIGARETTE TEST		
		NORMAL	BORDERLINE	ABNORMAL	NEGATIVE	BORDERLINE	POSITIVE
Normal Control							
20-39	70	68 (97.1%)	2 (2.9%)	0 (0.0%)	66 (94.7%)	4 (5.7%)	0 (0.0%)
40-49	69	56 (81.2%)	9 (13.0%)	4 (5.8%)	52 (75.4%)	14 (20.3%)	3 (4.3%)
50-59	62	22 (35.5%)	12 (19.4%)	28 (45.1%)	42 (67.8%)	11 (17.8%)	9 (14.4%)
> 59	51	9 (17.7%)	10 (19.6%)	32 (62.7%)	39 (76.5%)	5 (9.8%)	7 (13.7%)
TOTAL	252	155 (61.6%)	33 (13.1%)	64 (25.3%)	199 (79.0%)	34 (13.5%)	19 (7.5%)
Coronary Artery Disease							
20-39	24	15 (62.5%)	4 (16.7%)	5 (20.8%)	10 (41.6%)	5 (20.8%)	9 (37.6%)
40-49	58	18 (31.1%)	17 (29.4%)	23 (39.5%)	21 (36.2%)	10 (17.2%)	27 (46.6%)
50-59	67	12 (17.9%)	11 (16.4%)	44 (65.7%)	21 (31.3%)	14 (20.9%)	32 (47.8%)
> 59	41	2 (4.9%)	4 (9.8%)	35 (85.3%)	12 (29.3%)	4 (9.7%)	25 (61.0%)
TOTAL	190	47 (24.7%)	36 (18.9%)	107 (56.4%)	64 (33.7%)	33 (17.4%)	93 (48.9%)

The difference between the incidence of abnormal ballistocardiograms and positive smoking tests in the control and diseased groups is statistically significant in each decade.

No positive smoking test and no abnormal control pattern occurred in the normal subjects under the age of 40. A total of only three positive cigarette tests and four abnormal control tracings occurred in sixty-nine subjects in the fifth decade. Over the age of 50 there was a rapid rise in the incidence of control abnormality, although the smoking test was positive in less than 15 per cent.

In contrast, the patients with coronary artery disease showed a considerably higher incidence of abnormal form and of positive cigarette tests in each decade. Age has a definite influence, with an increasing incidence of abnormal form and an increasing frequency of positive smoking tests, occurring in each decade, although the effect on the latter is less striking. Patients with angina pectoris

responded to smoking in the same manner as those who had experienced a myocardial infarction, and no significant difference was found between the two classes of patients with coronary artery disease.

In order to evaluate the diagnostic usefulness of the ballistocardiogram, considering both the control pattern and the response to smoking, the total incidence, by decade, of abnormal resting form and/or positive cigarette test is summarized in Fig. 2. Under the age of 50 the striking difference between the control subjects and the patients is apparent, whereas over this age the difference becomes less significant.

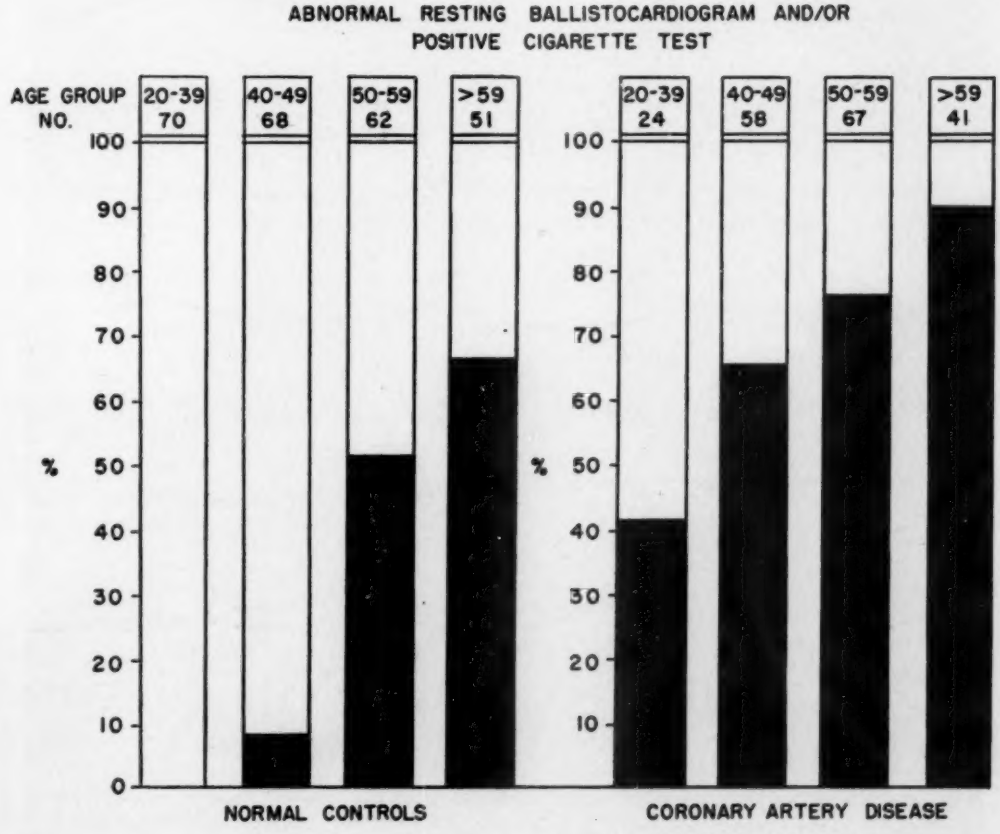

Fig. 2.—Graphic representation of abnormal resting ballistocardiograms and/or positive smoking tests in normal and coronary disease groups. The most striking difference occurs in subjects under the age of 50, whereas above this age the high incidence of abnormality in normal control subjects is readily apparent.

To determine the influence of previous smoking habits on the ballistocardiographic cigarette test, the incidence of positive tests was tabulated in two groups—those subjects who were habitual smokers and those who never smoked or had not smoked for several years. Table II summarizes these data, and it is clear that previous smoking habits have little or no influence on the results of this test. Inhalation and noninhalation likewise failed to play a significant role.

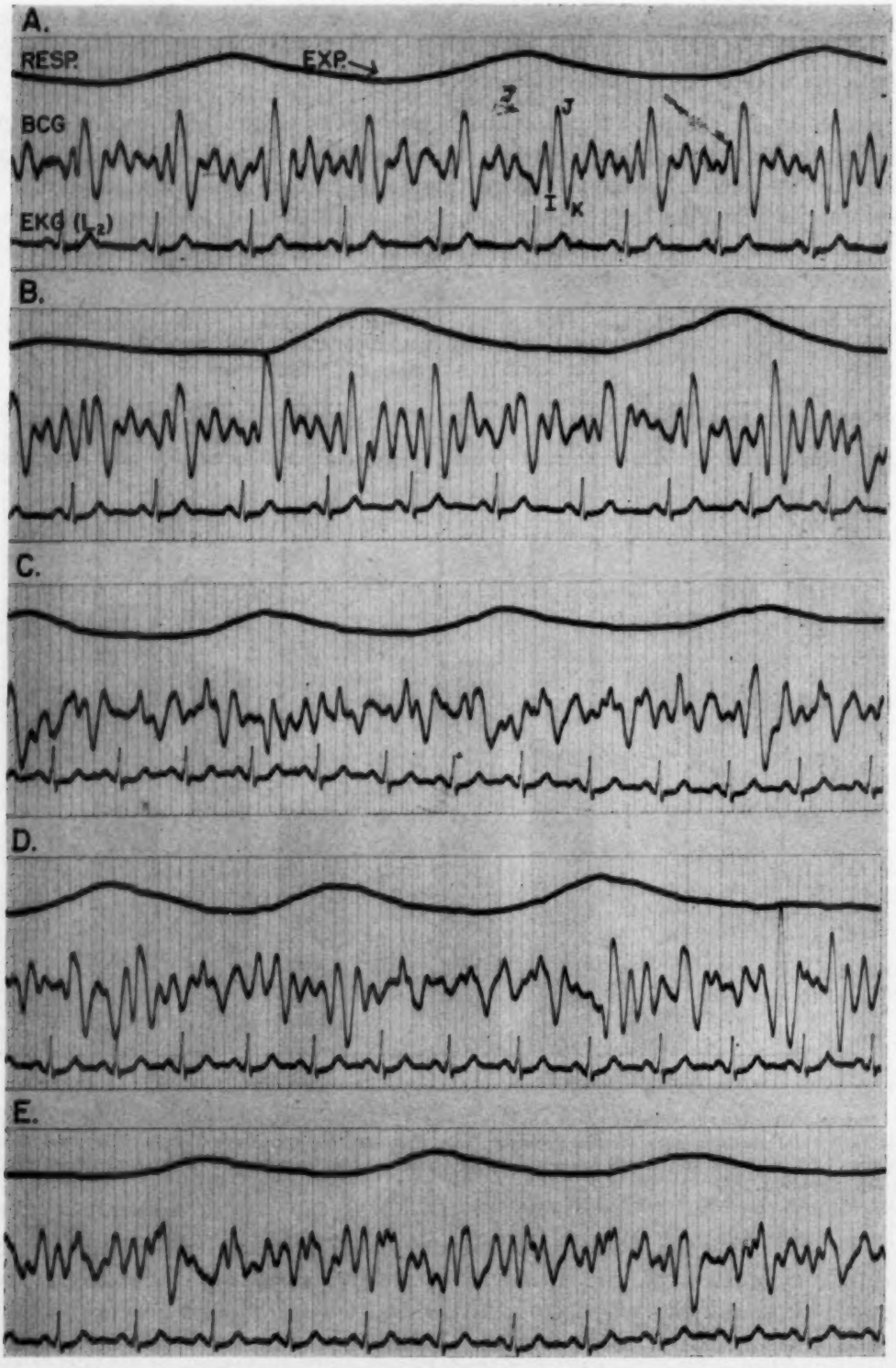

Fig. 3.—The effects of smoking on an apparently normal man, presented to show the temporal relationship between smoking and appearance of ballistocardiographic form alteration. *A*, Control record, which is within normal limits except for short expiratory I waves. *B*, Record thirty seconds after institution of smoking. Expiratory deterioration has begun to occur. *C*, Record two and one-half minutes after smoking has begun; gross distortion of all complexes is seen. *D* and *E*, Records immediately and five minutes after the completion of the cigarette; the prominent GH and systolic distortion remains readily apparent.

Table III summarizes the result of repeat tests in 159 subjects. Repeat performance is highly consistent in the person under 40 years of age. Over this age the variability of repeat response is somewhat greater. The greatest change occurred in the patients with coronary disease in the fifth decade, in which 33.3 per cent of the subjects showed an improved response. The interval between tests was many months, as tabulated, and few tests were performed within shorter intervals.

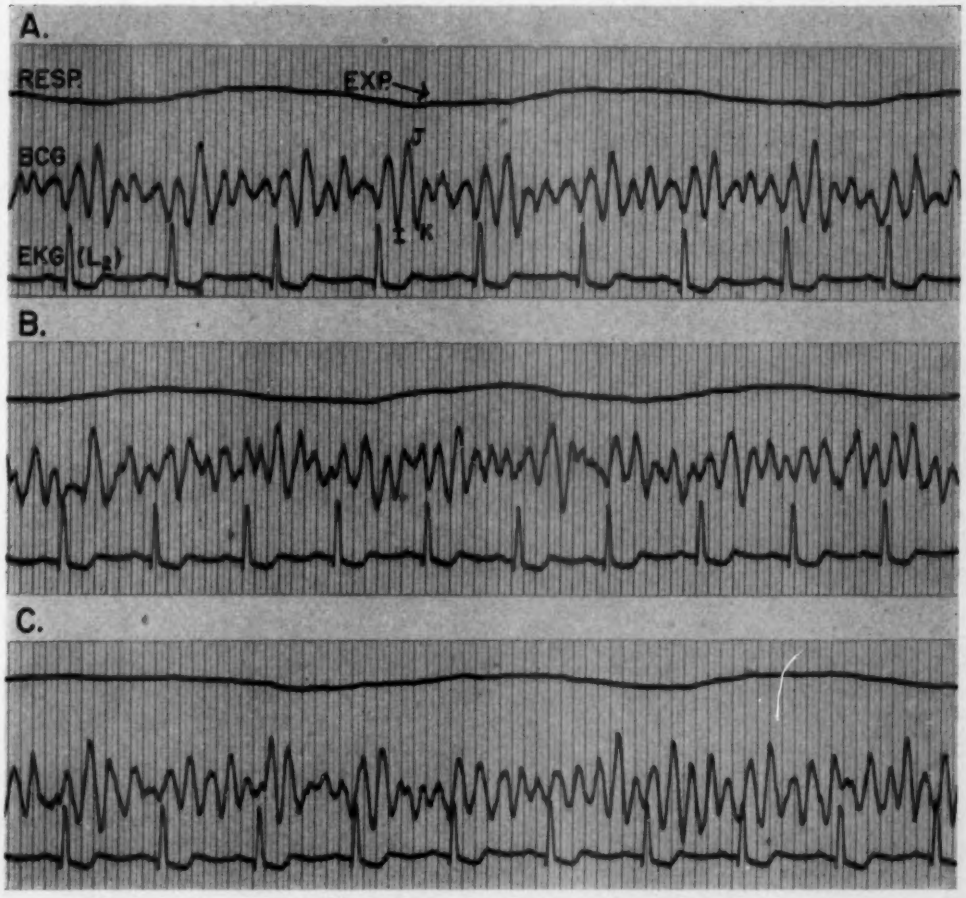

Fig. 4.—The cigarette test in a 73-year-old man with angina pectoris. *A*, Control record, which is slightly abnormal, primarily because of prominent GH. *B*, Record immediately after smoking. *C*, Record five minutes after smoking. The GH becomes relatively more prominent, diastolic waves increase, and there is variable systolic distortion. (See Fig. 5.)

In subjects who were studied during smoking, as well as immediately and five minutes after smoking, the alteration of form, when it occurred, often became apparent within thirty seconds after the institution of smoking. The usual pattern was that of increasing alteration of ballistocardiographic form so that the degree of change immediately after smoking was maximal. In only one subject was the distortion of pattern during smoking greater than that seen

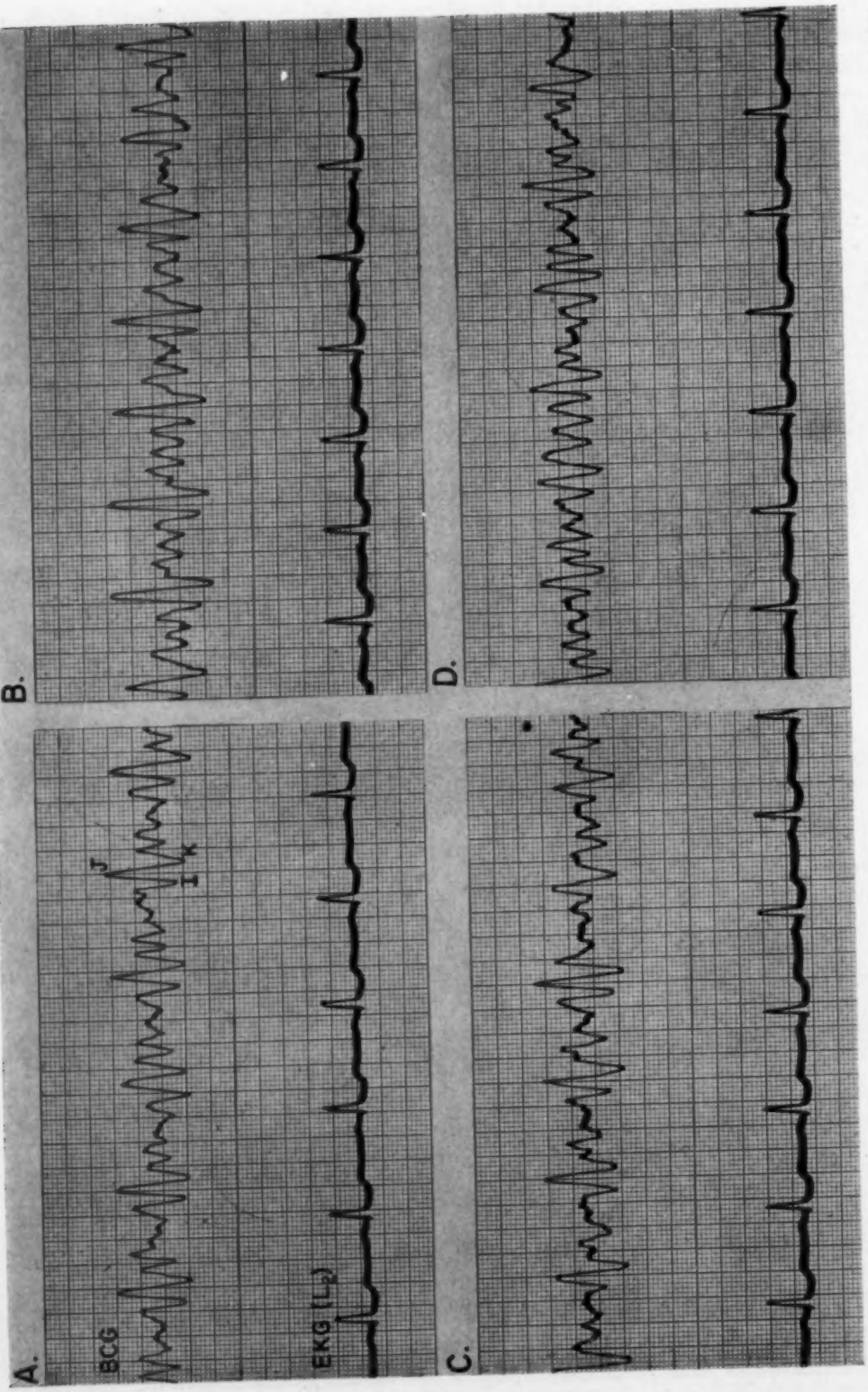

Fig. 5.—A cigarette test in the same patient shown in Fig. 4. *A*, Control record, which is generally similar to the control tracing in Fig. 4. *B*, Tracing four and one-half minutes after nitroglycerin and at the beginning of smoking. *C* and *D*, Records immediately and five minutes after smoking. The deterioration shown in Fig. 4 fails to occur, presumably because of the effect of nitroglycerin.

TABLE II. INFLUENCE OF SMOKING HABITS ON BCG RESPONSE

AGE	INCIDENCE OF POSITIVE TESTS							
	20 TO 39		40 TO 49		50 TO 59		> 59	
	SMOKER	NON-SMOKER	SMOKER	NON-SMOKER	SMOKER	NON-SMOKER	SMOKER	NON-SMOKER
Normal	48 (0.0%)	22 (0.0%)	44 (4.6%)	25 (4.0%)	45 (13.3%)	17 (17.6%)	36 (8.3%)	15 (20.0%)
Coronary disease	22 (36.4%)	2 (50.7%)	41 (48.8%)	17 (41.2%)	35 (48.6%)	32 (46.9%)	28 (57.2%)	13 (69.2%)

after completion of smoking. A few subjects showed slightly more alteration five minutes after smoking than immediately after.

Several types of filtered cigarettes have been tested. No filter, including a holder containing water-soaked pledgets, offered "protection" from the influence of smoking, as reflected by ballistocardiographic form alteration. Denicotinized cigarettes likewise failed to prevent this response.

In several subjects, nitroglycerin prevented the deterioration seen with smoking. Fig. 5 shows a representative case in which a positive response occurred before nitroglycerin, but a negative one occurred after the drug was administered.

TABLE III. RESULTS WITH REPEAT CIGARETTE TESTS

AGE	NUMBER OF SUBJECTS REPEATED	AVERAGE INTERVAL (MONTHS)	UNCHANGED	IMPROVED	NORMAL TO BORDERLINE	NORMAL OR BORDERLINE TO POSITIVE
Normal Controls						
20–39	20	15	19 (95.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)
40–49	28	16	20 (71.5%)	3 (10.7%)	2 (7.2%)	3 (10.7%)
50–59	32	19	18 (56.3%)	6 (18.7%)	6 (18.7%)	2 (6.3%)
> 59	22	19	14 (63.7%)	3 (13.6%)	4 (18.2%)	1 (4.5%)
Coronary Artery Disease						
20–39	5	12	5 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
40–49	21	16	10 (47.6%)	7 (33.3%)	3 (14.3%)	1 (4.8%)
50–59	22	11	16 (72.8%)	4 (18.2%)	0 (0.0%)	2 (9.0%)
> 59	9	10	8 (88.8%)	1 (11.2%)	0 (0.0%)	0 (0.0%)

In the few patients studied on the aperiodic bed, the form alteration occurred in a manner consistent with the change seen on the high-frequency bed, taking into consideration the differences in the basic pattern found with these two systems. Fig. 6 shows a representative response to smoking on the mercury bed.

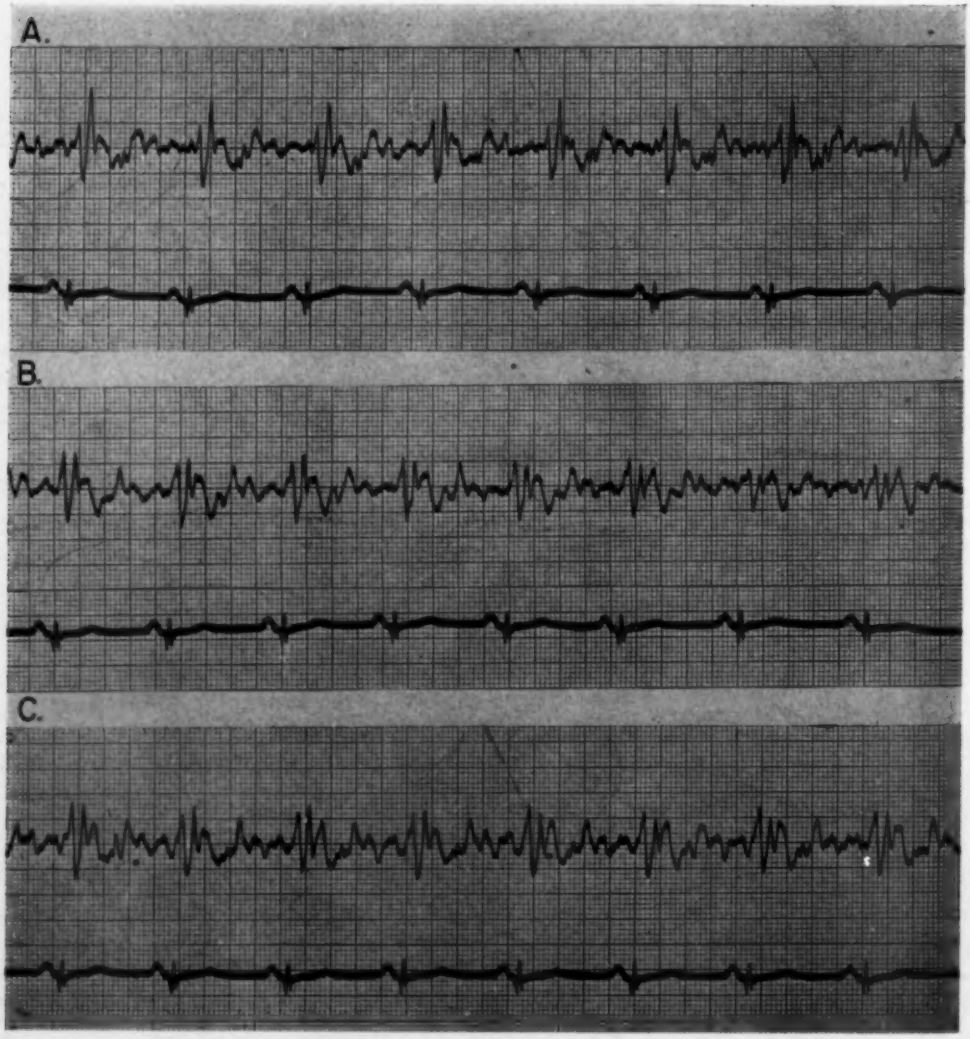

Fig. 6.—A cigarette test in a 45-year-old man with remote myocardial infarction. These records were obtained on the aperiodic (mercury) bed. *A*, Control record, within normal limits. *B*, Record immediately after smoking, showing relatively more prominent H waves, with diminished amplitude of J. *C*, Ballistocardiogram showing similar change, but of a lesser degree, five minutes after smoking. (These records from the mercury bed were obtained during suspended mid-respiration.)

DISCUSSION

Objectivity in the diagnosis of coronary insufficiency remains one of clinical medicine's most challenging problems. If a person develops what seems to be a myocardial infarction, and serial electrocardiograms are compatible with this

diagnosis, then the physician may justifiably conclude that no further objective evidence of his diagnosis is necessary. On the other hand, in the patient whose history suggests angina pectoris, particularly if the story is somewhat atypical, the diagnosis more often than not fails to be substantiated by some significant objective abnormality. The electrocardiogram is abnormal in only 24.1 per cent of such patients.[10] When the stress of exercise is added, the incidence of abnormality rises but, in our experience, the diagnostic discriminatory value of the two-step test is quite limited.[1]

The consideration of levels of blood lipids, in any one of several facets (namely, total cholesterol, cholesterol-phospholipid ratio, alpha-beta lipoprotein ratio, S_f 12-100 levels, etc.), is of value in group observations in subjects with coronary disease but is of very limited applicability to the individual patient. Anthropometric measurement is subject to the same criticism.

The ballistocardiogram has been widely studied, with the hope that it might add to the diagnostic armamentarium of the cardiologist, presenting him a means of developing further objectivity in his approach to the patient with diseased coronary arteries and facilitating discrimination between the person with true compromise of coronary flow and the person with chest pain of other origin. Seventy-five per cent of patients with clinically determined coronary artery disease have been found to have abnormal ballistocardiograms (at rest),[10] but the value of this high incidence of abnormality is limited by the 25.2 per cent of normal control subjects who also show abnormal tracings.[8] An attempt further to widen the gap between normal and disease groups by studying the ballistocardiograms after exercise was not sufficiently rewarding to warrant the application of this test to the clinic.[1]

In a previous report, we have shown that the ballistocardiographic cigarette test gave the most significant "diagnostic margin of differentiation", with the ballistocardiograms of 6.8 per cent of normal control subjects deteriorating after smoking, in contrast to 58.6 per cent of patients with coronary artery disease. The total number of individuals studied was 200. In the present report this series has been extended to 442 persons, and the general trends previously suggested have been confirmed. In the larger group it has become apparent that the difference between the frequency of positive cigarette tests in the control and diseased groups is not so great as previously reported, although a notable difference between these groups is again demonstrated. In the present study, 7.5 per cent of the normal persons showed a positive test, in contrast to 48.9 per cent of the patients with angina pectoris or remote myocardial infarction. The discriminatory ratio is thus 6.5:1, in contrast to the 9:1 ratio reported earlier. This ratio remains far greater than similar ratios of other objective methods known to us.

It is clear that, for clinical purposes, this test is of greatest value in subjects under the age of 50. No subject in the normal control group under 40 years of age showed ballistic deterioration after smoking, and only three of eighty-nine in the fifth decade had positive tests. All these positive tests in subjects under 50 years of age were in males. As an ancillary procedure in the study of patients with possible coronary disease (of clinically significant degree), the ballisto-

cardiographic cigarette test can thus be added to the diagnostic armamentarium in subjects under the age of 50 years. Above this age the frequency of positive tests, as well as abnormal resting tracings, is sufficiently great in the control group to necessitate great caution before applying the results to the study of an individual patient.

Repeat performance of the cigarette test is not, by any means, 100 per cent reliable. The most reproducible tests were in the younger subjects. It must be said, in defense of the procedure, that there were long intervals between tests and many alterations in the state of the myocardium could have occurred. Changes in the direction of improvement were more frequent in the patients with coronary artery disease. One could postulate, without any proof, that these subjects had established a more extensive collateral circulation, having withstood the stress of myocardial ischemia over a greater period of time. One necessarily wonders whether the extremely low fat diets on which some patients had been placed or the estrogenic substances which some had received might have played a modifying role. The period of observation is too short at the present time to allow these possibilities to be fully evaluated.

The basic mechanism by which cigarette smoking is frequently followed by alteration remains obscure. In a previous study it seemed that nicotine was the responsible agent.[1] Whether its effect on the ballistocardiogram is mediated through coronary or peripheral arterial constriction, by direct myocardial effect, or through some other mechanism, such as release of pitressin, is not clear. Ergonovine elicited somewhat similar deterioration in one subject. The only agent tested to date which has prevented the deterioration has been nitroglycerin, but whether this is due to a vascular or a myocardial effect cannot be stated with certainty. It is of interest, in this regard, that Russek and associates[6] found no significant protective effect with glyceryl trinitrate, but did find improved response after ingestion of whiskey. Limited observations in this laboratory on the effect of whiskey have not shown such a protective effect, but further observations in this regard would be of interest.

From the experience in this study, it would appear that the use of filters of various sorts or of "denicotinized" cigarettes is not a satisfactory means of preventing the ballistocardiographic response to smoking. Similar failure of filtered or "denicotinized" cigarettes to prevent deterioration was reported by Russek and associates[6] and Simon and associates.[5]

SUMMARY AND CONCLUSION

1. The effects of smoking on ballistocardiographic form in 252 normal subjects and 190 patients with coronary artery disease have been reported.

2. Abnormal resting ballistocardiograms were found in 25.3 per cent of normal control subjects and 56.4 per cent of patients with coronary disease.

3. The cigarette test was positive in 7.5 per cent of the control subjects, in contrast to 48.9 per cent of the coronary group.

4. Previous smoking habits, inhalation or noninhalation, and (in the group with coronary artery disease) presence of angina or previous myocardial infarction failed to influence the response of the ballistocardiogram to smoking.

5. No positive cigarette test occurred in control subjects under the age of 40; positive tests occurred in only three of eighty-nine subjects in the fifth decade.

6. Repeat cigarette tests were most consistent in persons under the age of 40. Variation of response in repeat tests was as great as 33.3 per cent in certain decades.

7. Maximal ballistocardiographic form change appeared in records obtained immediately after smoking in most subjects.

8. Filters of several types and the use of "denicotinized" cigarettes failed to prevent the ballistocardiographic alteration in normal or diseased subjects. Nitroglycerin prevented the deterioration in a few patients.

9. It is concluded that a positive ballistocardiographic cigarette test in a subject under the age of 50 suspected of having coronary artery disease might be considered ancillary evidence supportive of this diagnosis.

10. The ballistocardiogram and the ballistocardiographic cigarette test remain methods fraught with empiricism and are offered more as challenges to the clinical investigator than as routine procedures to be used freely in the clinic.

SUMMARIO IN INTERLINGUA

1. Es reportate le effectos del fumar super le forma ballistocardiographic in 252 subjectos normal e 190 patientes con morbo de arteria coronari.

2. Anormal ballistocardiogrammas de reposo esseva trovate in 25,3 pro cento del normal subjectos de controlo e in 56,4 pro cento del patientes con morbo coronari.

3. Le test a cigarettas esseva positive in 7,5 pro cento del subjectos de controlo e in 48,9 pro cento del patientes con morbo coronari.

4. Le reaction del ballistocardiogramma al fumar non esseva influentiate per previe habitudes de fumar, per inhalation o noninhalation, e (in le gruppo del patientes con morbo coronari) per le presentia de angina o le previe occurrentia de infarcimento myocardial.

5. Le test a cigarettas esseva positive in nulle subjecto de controlo infra le etate de 40 annos. Illo esseva positive in solmente tres ex octanta-nove subjectos in le quinte decennio.

6. Secunde tests a cigarettas se monstrava le plus uniforme in personas infra le etate de 40 annos. Variationes del responsa in secunde tests amontava in certe decennios a 33,3 pro cento.

7. In le majoritate del casos le alterationes maximal del forma ballistocardiographic appareva in registrationes obtenite immediatemente post le fumar.

8. Filtros de varie typos e le uso de cigarettas "disnicotinisate" preveniva le alterationes ballistocardiographic ni in subjectos normal ni in le patientes. Nitroglycerina preveniva le deterioration in alicun patientes.

9. Nos conclude que un positive test ballistocardiographic a cigarrettas in individuos infra le etate de 50 annos pote esser considerate como supporto ancillari de un alteremente suspicite diagnose de morbo del arteria coronari.

10. Le ballistocardiogramma e le test ballistocardiographic a cigarrettas remane methodos impregnate con empiricismo. Illos es presentate como stimulation pro le investigator plus tosto que como procedimentos routinari de libere uso clinic.

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PHYSICAL BASIS OF BALLISTOCARDIOGRAPHY. III

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INTRODUCTION

BY MEANS of a ballistocardiograph (BCG) record is made of the displacement, the velocity, or the acceleration with which the center of gravity of the subject moves because of the action of the heart. The subject lies on a BCG, and the displacement, the velocity, or the acceleration of subject or BCG is recorded. From these curves something is to be detected about the occurrences within the body. The type of BCG that is made use of determines which quantity concerning the center of gravity is represented by the recorded curve. These relations were dealt with in preceding papers.[2,3] Summarized, these relations are:

1. The displacement of a *low-frequency* BCG, damped critically or somewhat less than critically (natural frequency about or less than 0.3 c/s), represents the displacement of the center of gravity of subject and BCG caused by the circulation.

2. The displacement of a *middle-frequency* BCG (natural frequency about 1 to 2 c/s) represents the velocity of the center of gravity, provided that the damping is much more than critical.

3. The displacement of a *high-frequency* BCG (natural frequency of the loaded BCG about 15 c/s) represents the acceleration of the center of gravity of subject and BCG reliably up to about 10 c/s. (The internal force is to be found by means of multiplication of the acceleration and the mass.)

In the deduction of these relations it was assumed that the binding between the body of the subject and the BCG were infinitely strong. We remarked that in reality this binding is far from this extreme case.[2,3] So the movement of the subject differs from the movement of the BCG and that difference is greater the higher the frequency that is to be represented.

Nickerson and Mathers[1] give formulas by which they calculate how the representation of the forces that cause the center of gravity to move are distorted if (a) the displacement of the high-frequency BCG or (b) the displacement of their "low-frequency" BCG is recorded. We call this type of BCG the middle-frequency BCG, because the natural frequency of this type is neither high nor low with respect to the frequency of the heart. The type used by us has a considerably lower natural frequency. We will call the latter the low-frequency BCG.

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THEORY

In its simplest form the problem of the relative movement is a special case of a more general problem: that of two coupled harmonic oscillators.

The problem in the form we have to face it can schematically be represented in the form of Fig. 1. The subject with the mass m_s is represented by a cart that is coupled to the BCG with mass m_b by a directive force and a frictional force. The system of subject and BCG is in the same way coupled to the surroundings.

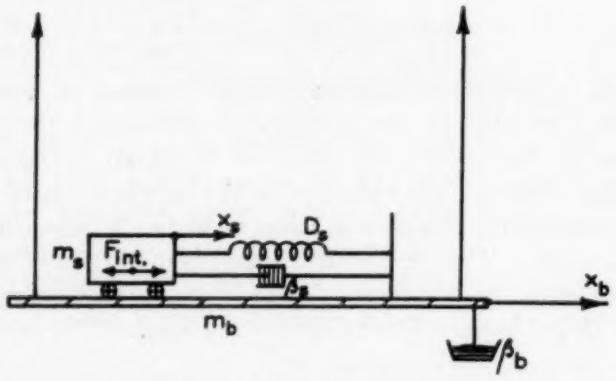

Fig. 1.—Schematic representation of the ballistocardiographic system in which the relative movement is taken into account. The subject with mass m_s is coupled to the BCG with mass m_b by a directive force and a frictional force. The whole system is coupled to the surroundings in an analogous way.

Nickerson and Mathers do not give the deduction of their formulas to calculate the distortion, but refer to a textbook.[4] From this we deduced that they reasoned as follows. Suppose that the movement of the BCG does not influence the movement of the subject. Then, the distortion caused by the vibration properties of the subject can be calculated from the differential equation:

$$m_s \ddot{x}_s + \beta_s \dot{x}_s + D_s x_s = F_{int} \tag{1}$$

x_s, $\dot{x}_s$ and $\ddot{x}_s$ are the respective displacement, velocity, and acceleration of the body with mass m_s with respect to the fixed BCG. $D_s x_s$ is the directive force acting between subject and BCG that drives the subject to the zero position on the BCG; $\beta_s \dot{x}_s$ is the frictional force between subject and BCG. F_{int} is the internal force that causes the center of gravity to move.

From equation (1) follows the relation between the amplitudes of the internal force $|F_{int}|$ and the amplitude of the displacement of the subject $|x_s|$:

$$\frac{|x_s|}{|F_{int}|} = \frac{1}{[(m_s\omega^2 - D_s)^2 + \beta_s^2\omega^2]^{\frac{1}{2}}} \tag{2}$$

($\omega = 2\pi\nu$, ν the frequency of a term of the Fourier expansion, in which the phenomena can be developed). By the movement of the subject a force F_{tr} is exerted on the BCG:

$$F_{tr} = D_s x_s + \beta_s \dot{x}_s \tag{3}$$

with the amplitude $|F_{tr}|$

$$|F_{tr}| = |x_s|[D_s^2 + \beta_s^2\omega^2]^{\frac{1}{2}}. \tag{4}$$

Equation (2) substituted in equation (4) gives the relation between the amplitudes of the force exerted on the BCG $|F_{tr}|$ and of the internal force $|F_{int}|$ thus gives the distortion of $|F_{int}|$ by the vibration properties of the subject:

$$\frac{|F_{tr}|}{|F_{int}|} = \left[\frac{D_s^2 + \beta_s^2\omega^2}{(m_s\omega^2 - D_s)^2 + \beta_s^2\omega^2}\right]^{\frac{1}{2}}. \tag{5}$$

Equation (5) can be written in another form

$$\frac{|F_{tr}|}{|F_{int}|} = \left[\frac{1 + 4\delta_s^2\dfrac{\nu^2}{\nu_s^2}}{\left(1 - \dfrac{\nu^2}{\nu_s^2}\right)^2 + 4\delta_s^2\dfrac{\nu^2}{\nu_s^2}}\right]^{\frac{1}{2}}. \tag{5a}$$

ν_s is the natural frequency of the subject on the fixed BCG; it is the frequency with which the subject would oscillate if there were no damping ($\beta_s = 0$). δ_s is the ratio of the damping β_s and the critical damping of the subject on the fixed BCG. So $\delta_s = 1$, if the damping of the subject with respect to the BCG is critical. The form on the right side of equation (5a) is called Ta by Nickerson and Mathers. So, in their notation:

$$|F_{tr}| = \text{Ta}\ |F_{int}|. \tag{5a}$$

The distortion caused by the vibration properties of the BCG can, according to Nickerson and Mathers, be calculated from a differential equation analogous to equation (1):

$$m_b\ddot{x}_b + \beta_b\dot{x}_b + D_bx_b = F_{tr} \tag{6}$$

In this equation x_b, $\dot{x}_b$ and $\ddot{x}_b$ are the respective displacement, velocity, and acceleration of the BCG with respect to the surroundings. The mass of the BCG itself is m_b. The frictional force with respect to the surroundings is $\beta_b\dot{x}_b$ and the directive force is D_bx_b.

If the amplitude $|x_b|$ of the displacement x_b is recorded, the distortion of $|F_{tr}|$ is:

$$\frac{|x_b|}{|F_{tr}|} = \frac{1}{[(m_b\omega^2 - D_b)^2 + \beta_b^2\omega^2]^{\frac{1}{2}}}. \tag{7}$$

Equation (7) can be written in the following form:

$$\frac{|x_b|}{|F_{tr}|} = \frac{1}{m_b\omega_b^2}\ \frac{1}{\left[\left(1 - \dfrac{\nu^2}{\nu_b^2}\right)^2 + 4\delta_b^2\dfrac{\nu^2}{\nu_b^2}\right]^{\frac{1}{2}}}. \tag{7a}$$

$m_b\omega_b^2$ is a constant, so this distortion is given by

$$\text{Ra} = \frac{1}{\left[\left(1 - \dfrac{\nu^2}{\nu_b^2}\right)^2 + 4\delta_b^2\dfrac{\nu^2}{\nu_b^2}\right]^{\frac{1}{2}}}. \tag{7b}$$

The symbol Ra is used by Nickerson and Mathers.

In formula (7b) ν_b means the natural frequency and δ_b the ratio of the damping β_b and the critical damping of the *unloaded* BCG. The formulas (7a) and (7b)

do not hold good in case the BCG is suspended on wires as usually happens with the low-frequency BCG. This follows from the fact that D_b in formula (7) means the external force necessary to give the loaded BCG a deflection of 1 cm. In this case D_b can be calculated from

$$2\pi\nu_b' = \left[\frac{D_b}{m_s + m_b}\right]^{\frac{1}{2}}. \tag{8}$$

ν_b' is the natural frequency of the loaded BCG and is usually with good approximation independent of the load, just as with a pendulum.

If the BCG is mounted on springs, the same D_b can be found from

$$2\pi\nu_b = \left[\frac{D_b}{m_b}\right]^{\frac{1}{2}} \tag{9}$$

in which ν_b is the natural frequency of the unloaded BCG (because of the fact that ν_b depends on the mass m_s).

From equations (5) and (7) the total amplitude distortion, according to Nickerson and Mathers, follows:

$$\frac{|x_b|}{|F_{int}|} = \left[\frac{D_s^2 + \beta_s^2\omega^2}{\{(m_s\omega^2 - D_s)^2 + \beta_s^2\omega^2\}\ \{(m_b\omega^2 - D_b)^2 + \beta_b^2\omega^2\}}\right]^{\frac{1}{2}}. \tag{10}$$

Written in their notation:

$$\frac{|x_b|}{|F_{int}|} = \frac{1}{m_b\omega_b^2}\ \text{Ta. Ra.} \tag{10a}$$

Schematizing as has been described already (Fig. 1) we ourselves calculated among other things the distortion in the representation of the amplitude of the internal force if the displacement of the BCG is recorded. In this calculation the influence of the movement of the BCG on the movement of the subject is taken into account.[5] We found:

$$\frac{|x_b|}{|F_{int}|} = \left[\frac{D_s^2 + \beta_s^2\omega^2}{p^2 + q^2}\right]^{\frac{1}{2}}. \tag{11}$$

From this calculation follow p and q:

$$p = m_s m_b\omega^4 - \omega^2(m_s D_b + m_b D_s + m_s D_s + \beta_s\beta_b) + D_s D_b$$
$$q = -\omega^3(m_s\beta_b + m_b\beta_s + m_s\beta_s) + \omega(\beta_s D_b + \beta_b D_s).$$

Nickerson and Mathers[1] give a formula for the phase shift analogous to formula (10a). We[5] calculated the phase shift analogously to the calculation of formula (11). This problem will not be discussed here.

COMPARISON OF THE RESULTS OBTAINED WITH THE CORRECT CALCULATION AND THE APPROXIMATION OF NICKERSON AND MATHERS

The curves in Figs. 2 and 3 represent the distortion according to formula (10a) of Nickerson and Mathers, interpreted in the correct manner (especially concerning ν_b and δ_b, see above), and those according to our formula (11).

To obtain Figs. 2 and 3, we substituted in formula (10), which is identical with formula (10a), and in the formula (11), the following data:

m_s = 60 kg.
m_b = 15 kg., according to data given by Starr (Nickerson and Mathers give no data about m_b).
$D_s = 38.10^6$ g.cm^{-2}, calculated with the aid of

$$2\pi\nu_s = [D_s/m_s]^{\frac{1}{2}}.$$

In this formula $\nu_s = 4.0$ c/s, according to the measurements of Nickerson and Mathers[1] and ours.[5]

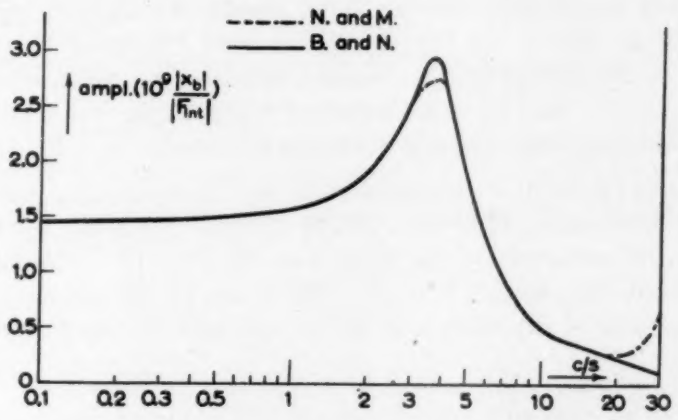

Fig. 2.

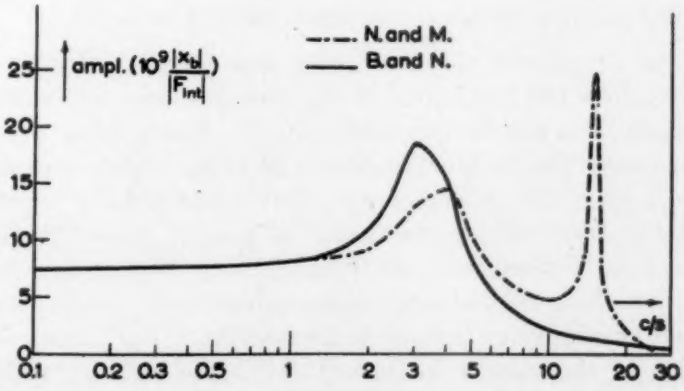

Fig. 3.

Fig. 2.—Amplitude characteristics of a high-frequency BCG (natural frequency of the *loaded* BCG 15 c/s) calculated according to the method of Nickerson and Mathers (broken line) and according to the authors' method (solid line).

Fig. 3.—Amplitude characteristics of a high-frequency BCG (natural frequency of the *unloaded* BCG 15 c/s) calculated according to the method of Nickerson and Mathers (broken line) and according to the authors' method (solid line).

Nickerson and Mathers measured $\delta_s = 0.2$. This accords with part of our measurements done under special conditions. We will take a somewhat different value of δ_s, namely, $\delta_s = 0.3$, from which follows $\beta_s = 10^6$ g.sec^{-1}, a number near the mean of all measurements. From a paper of Bouhuys[6] it follows that $\beta_b = 85.10^3$ g.sec^{-1}. This means $\delta_b = 14.10^{-3}$. We have chosen this number, which is much lower than the data used by Nickerson and Mathers,

because the high-frequency BCG usually is, as far as we know, damped to this extent. (The damping of a BCG can be calculated directly from a curve representing the movement of the BCG carrying a load that is fixed to the BCG if the BCG is released without initial velocity from a position that is not the zero position. If the BCG carries a load that is not fixed to the BCG (e.g., a subject), then the damping of the BCG differs from the above-mentioned case.[6] The coefficients β_b and D_b from the formulas (10) and (11) mean those from the fixed load).

To complete the necessary data we have chosen different values of the natural frequency of the BCG. In Fig. 2 we have used a value of 15 c/s for the natural frequency of the *loaded* BCG. From this it follows with equation (8) that $D_b = 68.10^7$ g.sec^{-2}. In Fig. 3 we assumed the natural frequency of the *unloaded* BCG to be 15 c/s. So, $D_b = 136.10^6$ g.sec^{-2}.

From Fig. 2 it appears that the amplitude characteristics do not agree so badly for higher frequencies. However, if the natural frequency of the BCG approaches the natural frequency of the subject on the fixed BCG, the agreement is worse, also for lower frequencies (Fig. 3). Then the amplitude characteristic obtained by the method of calculation of Nickerson and Mathers is unreliable.

THE CURVES CONCERNING THE MIDDLE-FREQUENCY BALLISTOCARDIOGRAPH

Nickerson and Mathers also calculate the distortion appearing when a middle-frequency BCG is used (natural frequency about 1 to 2 c/s).

To calculate the amplitude distortion they use formula (10a). In other words, they calculate how the amplitude of the internal force is distorted if one records the amplitude of a middle-frequency BCG. Apart from the influence of the relative movement, the middle-frequency BCG has only a suitable amplitude characteristic and phase characteristic if its amplitude is regarded as a measure of the velocity with which the center of gravity moves.[2,3] But then, the loaded BCG must be damped far more than critical. Nickerson and Mathers damp their BCG less than critical and make calculations concerning the acceleration of the center of gravity instead of its velocity. For these two reasons their characteristics of the middle-frequency BCG are difficult to interpret.

Nickerson and Mathers give two curves regarding the middle-frequency BCG (their Fig. 1). In one of these cases the calculation is not correct, for they substitute for ν_b and δ_b of formula (10a) the data belonging to the *loaded* BCG (curve E).

SUMMARY

Two methods for calculating the amplitude characteristic of the high-frequency BCG, the difference in movement of subject and BCG taken into account, are compared and discussed.

Some remarks are made upon the calculation of the amplitude characteristic of the middle-frequency BCG according to Nickerson.

SUMMARIO IN INTERLINGUA

Es comparate e discutite duo methodos de calcular le amplitude characteristic del ballistocardiographo a alte frequentia, con consideration del differentia del movimento de subjecto e ballistocardiographo.

Es facite alicun remarcas in re le calculation del amplitude characteristic del ballistocardiographo a frequentia median secundo le methodo de Nickerson.

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THE RELATIVE VALUE OF ELECTROCARDIOGRAPHY AND PHOTOROENTGENOGRAPHY FOR CARDIAC SURVEYS

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AUGUSTA, GEORGIA

A MASS survey method for the detection of any disease should be rapid, cheap, and require minimal technical skill in securing records. For reasons of economy, interpretation of records should require a minimum of professional time. Finally, this method should yield a high percentage of cases of the disease under study, and of equal importance, must not suggest disease where none exists. This is particularly important since the principle purpose of mass surveys is to eliminate expensive examination of patients who eventually are found to be disease free. These criteria are adequately satisfied by mass survey x-rays for tuberculosis. No completely satisfactory method, however, has yet been devised for cardiac surveys.

An excellent recent evaluation of the relative values of techniques for heart disease indicates that 12-lead electrocardiography is the best single technique in cardiac case finding.[1] It has, however, the almost prohibitive disadvantage of being too time-consuming and, in addition, indicts a large number of normal people. About two-thirds of known cardiacs are detected with the usual methods of interpretation. The mass survey x-ray detects far fewer cases of known cardiacs, but does not cause nearly so many false positives.[1-5] Questionnaires show up badly in such controlled studies because of the nonspecificity of cardiac complaints.[1] A special device for simultaneously recording an electrocardiographic lead, a Dock type ballistocardiogram, and an electrokymogram has been suggested for mass surveys.[6] This device has not yet been evaluated, but does not appear to be promising in view of the care required to secure the records and because the value of either single lead electrocardiography or electrokymography alone is disappointing.[1,6] To our knowledge, the simple technique of direct body ballistocardiography has also not been tested for this purpose, but does not seem to be a fruitful line of investigation because of the unknown significance of unsupported ballistocardiographic abnormalities, especially in older populations. It is well known, moreover, that normal ballistocardiograms may

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be found in many cases of congenital heart disease and chronic valvular disease.[7] Mass phonocardiography has been of interest to us and others,[8] but fails on many of the criteria listed above. Mass examinations by physicians with emphasis on inspection, auscultation, and sphygmomanometry has been largely a failure in our hands because of the rapid loss of efficiency due to examiner fatigue, and because it is too time-consuming and requires highly trained professional personnel.[9]

From the above brief survey of available methods, it appeared that only two, electrocardiography and mass roentgenography, held any promise. Either alone, however, had many drawbacks. Few cardiacs, however, have both a normal ECG and x-ray. The possibility was suggested, therefore, that a combination of these methods might well enhance the detection rate over either alone without necessarily increasing the number of false positives among noncardiacs. This possibility seemed worth testing when in the course of a survey of a large hospital population, a 4-lead electrocardiographic method was developed with a detection rate not appreciably less than that for the full 12 leads.[9,10] After streamlining the techniques for securing these tracings, it was found that although the number of necessary nonprofessional personnel was increased, almost as many patients per hour could be studied by both methods as by either alone.

MATERIAL AND METHODS

In order to test this hypothesis, it was necessary to apply the above techniques to a patient population in which the diagnosis was firmly established. In order to encompass a representative diagnostic spectrum, it was necessary to select cases. It was decided to collect twenty-five consecutive patients with heart disease seen by the cardiology service in each of five diagnostic categories —arteriosclerotic, hypertensive, rheumatic, congenital without obvious cyanosis, and a miscellaneous group of unusual or secondary forms of heart disease. As a control, 100 "normal" individuals were treated in the same manner. No attempt was made to select a control group comparable in age and sex to that contained in the pathologic group. It was thought that the difficulty in evaluating the significance of minor changes in the electrocardiograms and photoroentgenograms of the older age group would negate whatever might be gained by age selection. Approximately half of the control group were professional or technical hospital personnel without signs, symptoms, or historical evidence of heart disease. All who showed questionable electrocardiograms or x-rays were subjected to whatever procedures were necessary to decide whether or not heart disease existed. The other half were chosen consecutively from medical service in-patients with noncirculatory diseases. After records on the entire group of 225 cases had been taken, seven were "thrown out" because of technical imperfections in the records or because the examiners could not be completely certain whether heart disease did or did not exist in mild form. Careful re-evaluation of each case after all data had been studied, resulted in a change in diagnosis in a few cases so that the distribution into diagnostic categories was not as equal as originally intended. A few cases, for example, were discovered to have more than one etiological type of heart

disease and were, therefore, either excluded from the series or if, in the opinion of the examiners, the manifestations of the disease seemed to be unquestionably caused by only one etiological type, they were classified into that category. The decision as to whether some cases did or did not have heart disease was more difficult than anticipated, particularly in the "miscellaneous" group where systemic diseases which often, but not always, cause cardiac involvement were present. In these cases, heart disease was defined as "not only the structural changes found in the heart, pericardium, and adjacent arterial structures, but also such disturbances of the functions of the heart as manifested by arrhythmia, by its ability to perform its function as a pump, and by its tendency to give rise to abnormal sensations."[11] This final classification resulted in 23 cases diagnosed as arteriosclerotic heart disease, 26 as rheumatic, 26 as congenital, 31 as hypertensive cardiovascular disease, and 21 in the miscellaneous group. Ninety-two cases were thought to have no heart disease. The miscellaneous group of cardiopathies included 2 with disseminated lupus, 2 cor pulmonale, 6 Graves' disease, 4 syphillis, 2 acromegaly, 1 beriberi, 1 scleroderma, 1 secondary anemia, 1 nonspecific myocarditis, and 1 sickle cell heart disease. The congenital group contained 8 with auricular septal defects, 7 ventricular septal defects, 5 patent ductus arteriosus, 1 subaortic stenosis, 1 undifferentiated septal defect, 1 bicuspid aortic valve, 1 noncyanotic tetralogy of Fallot,[12] 1 coarctation of the aorta, and 1 isolated right aortic arch. Criteria for diagnosis was that of the New York Heart Association.[11]

Leads I, aV_F, a midsternal V lead, and a mid-axillary V lead at the same level was taken on each patient as previously described.[9,10] Criteria for interpretation was also that used in the description of this method with one exception—the normal limits for "left ventricular potential" were thought to be too narrow in view of the findings in the present group of normals and in another series.[9] A better separation between normals and abnormals was obtained if a sum of R V lateral plus S V anterior of 38 mm. was considered the upper limits of normal. A few exceptions to the original voltage criteria of Sokolow and Lyon on the 12-lead electrocardiogram have been found by us and others.[9,13] As will be seen later, they were found in the present series even with the more liberal "normal" range.

Photoroentgenograms (4 by 5 inch PA) were taken on each patient. Tube to chest distance was 42 inches. Height and weight were obtained on all. The transverse diameter of the heart was measured on the minifilm and multiplied by 3.7, so that the results could be applied to the tables for the prediction of transverse diameter prepared by Ungerleider and Clark.[4,14] At first, the internal diameter of the chest was measured at the level of the diaphragmatic attachment, so that a "cardiothoracic ratio" could be estimated. Because of disagreement among the authors as to where this measurement should be made on a number of cases, and lack of reproducability of the ratios on others, it was decided that the figures derived from such data would probably be worthless and the method was abandoned. The reasons for the inadequacy of this technique have been discussed elsewhere.[4,15,16] Cardiothoracic ratio is, however, such an easily obtainable figure that it was thought worthwhile that it be obtained in a different manner and test the

results. Accordingly, the internal diameter of the chest was measured at the level of the fourth intercostal space anteriorly. This suggestion was introduced into the medical literature by Meneely and has to our knowledge never been adequately tested.[17] If worthwhile, the cardiothoracic ratio would have a distinct advantage over the prediction tables because no measurement of the height and weight is required. The fact that this index of heart size correlates fairly well with independently derived, but related physiological data presents some internal evidence that it is a reasonably valid measurement.[18]

The problem of interpreting cardiac silhouettes for mass survey purposes is quite different from that in diagnostic cardiology. In the latter case, no harm is done and sometimes distinct aid is rendered by the radiologist who "suspects" abnormality. On the other hand, the mass survey radiologist must categorically state that the heart is either normal or abnormal. If he states that it is normal while the patient actually has heart disease, his confreres usually never learn about the mistake and he escapes criticism. If he reads the film with the same degree of suspicion as the diagnostic radiologist, however, each record that he labels as "abnormal heart" will call for careful examination of that patient to test his contention. If many such cases are normal, he will not be looked upon with favor. From the fact that very few false positive x-ray readings have been reported in such surveys in the past, it is suggested that this was often the quite understandable approach of the radiologist. It may also account in part, however, for the rather poor detection rates reported in some series. These range between 4 and 44 per cent and false positives from less than 1 to slightly over 2 per cent.[1-5,19]

In this study, a different approach was tried and "suspicious" silhouettes were labeled "abnormal" even in the absence of cardiac enlargement. This usually means an interpretation of the left cardiac border which, of course, has a high degree of variability in the normal. For this study, the diagnosis of "concentric hypertrophy" of the left ventricle without an increased transverse diameter of the heart was not made. The remaining possibilities are subjective evaluations of the aortic shadow, calcifications, straightening of the left border, the pulmonary artery, and the left auricular appendage.

RESULTS

1. *Electrocardiogram.*—Table I lists the electrocardiographic diagnoses in the 126 cardiacs and the ninety-two normals. The rather unsatisfactorily high number of false positives (11 per cent) among the normals was mainly a result of so-called "minor" electrocardiographic abnormalities. A glance at the large number of minor abnormalities among the cardiacs indicates that if these diagnoses were disregarded, the percentage of cardiacs detected by the electrocardiographic method would fall precipitously. These findings are in accord with those of others.[1,20,21]

2. *X-ray.*—Figs. 1 and 2 illustrate the separation of cardiacs and noncardiacs by the two objective methods of estimating cardiac enlargement. The line arbitrarily used to separate normals from abnormals is at the point suggested

by Ungerleider and Clark in one instance (Fig. 1) and by the best separation in the present series in the second (Fig. 2). A comparison shows that a somewhat better separation was obtained by measuring the cardiothoracic ratio (C/T ratio) in the manner described, since approximately the same number of cardiacs was detected and the number of false positives was distinctly less.

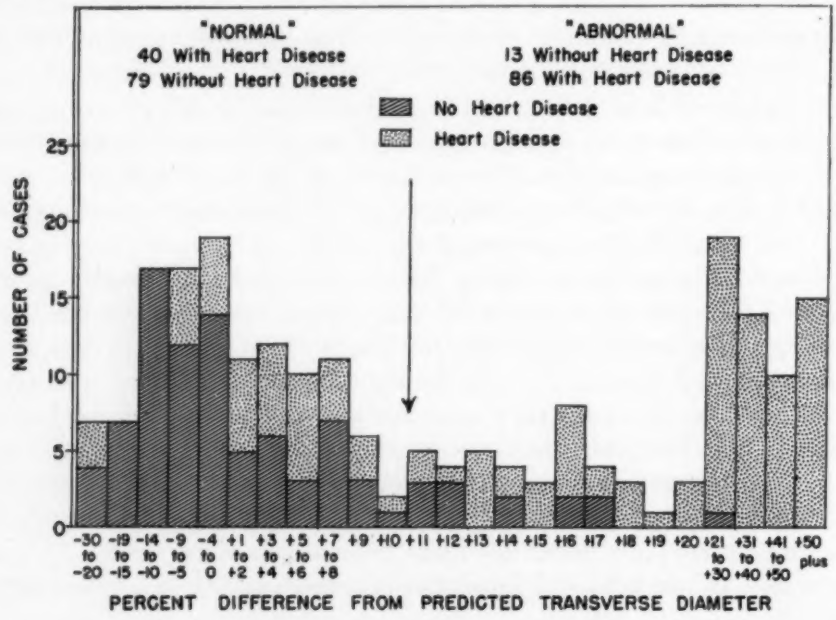

Fig. 1.—Two hundred and eighteen cases divided according to percentage deviation from their cardiac transverse diameter as predicted from the tables of Ungerleider and Clark. A transverse diameter greater than 10 per cent above the expected is considered "abnormal."

TABLE I

ELECTROCARDIOGRAPHIC DIAGNOSIS	HEART DISEASE	NORMAL
LVH—abnormal activation time	38	0
LVH—increased voltage only	19	2
Isolated ST-T abnormality	11	3
RBBB, complete or incomplete	11	1
LBBB	2	0
RVH	11	3
Auricular fibrillation	5	0
Combined hypertrophy	3	0
Heart block, incomplete	1	0
Miscellaneous	3	1
TOTAL	104	10

Table II lists the radiologic diagnoses made on both the normal and abnormal groups. It will be seen that, as expected, most cases with heart disease detected by the x-ray method had cardiac enlargement and conversely, cardiac enlargement was the most reliable sign of heart disease. The diagnosis of an abnormal heart in the absence of cardiac enlargement was indeed hazardous. When x-rays were

read without measurement, but only in respect to the visual impression of cardiac enlargement, there was no significant fall in the detection rate, and relatively little change in the number of false positives which is satisfactorily low by either technique. This tends to support the hypothesis that most radiographic interpretation of survey films is dependent on the presence of cardiac enlargement. It

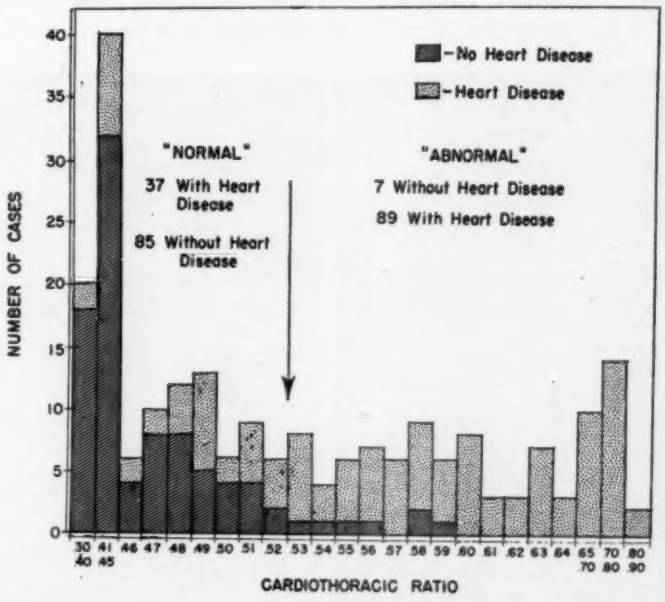

Fig. 2.—Two hundred and eighteen cases divided according to their cardiothoracic ratios. Internal diameter of the chest measured at the level of the fourth anterior intercostal space. The best separation of cardiacs and noncardiacs is at a C–T ratio of 0.52, and any measurement above this figure is considered "abnormal."

goes without saying that most cases with cardiac enlargement also showed abnormal contours, but the impression of an abnormal contour was so strengthened by a definite increase in the transverse diameter of the heart that it appears quite possible that most mass radiographers, consciously or unconsciously, would fail to report unusual contours unless their suspicions were supported by cardiomegaly. As previously discussed, there are excellent reasons for this caution.

TABLE II

X-RAY IMPRESSION	CARDIACS (126)		NORMALS (92)	
Cardiac enlargement				
Visual impression	86	(68%)	4	(4%)
Ungerleider-Clark tables	86	(68%)	13	(14%)
Cardiothoracic ratio	89	(71%)	7	(8%)
Prominent Pulmonary Conus*	9	(7%)	6	(6.5%)
Straight left border*	2	(1.6%)	5	(5.4%)
Abnormal aortic shadow*	8	(6%)	2	(2%)
Aortic calcification*	0		1	(1%)

*No visual impression of cardiac enlargement and C/T ratio <.53.

Figs. 3*A* and 3*B* illustrate eight cases whose x-rays show "fullness of the pulmonary artery", or "straightening of the left border" ("mitralization" of the heart). By both methods of measurement, there was no cardiac enlargement and without this aid, it was obviously quite difficult to differentiate pathology from a normal variant. In fact, some of the "suspicious" contours may have been associated with heart disease purely by coincidence in view of the fairly high incidence of the same findings in the normal group.

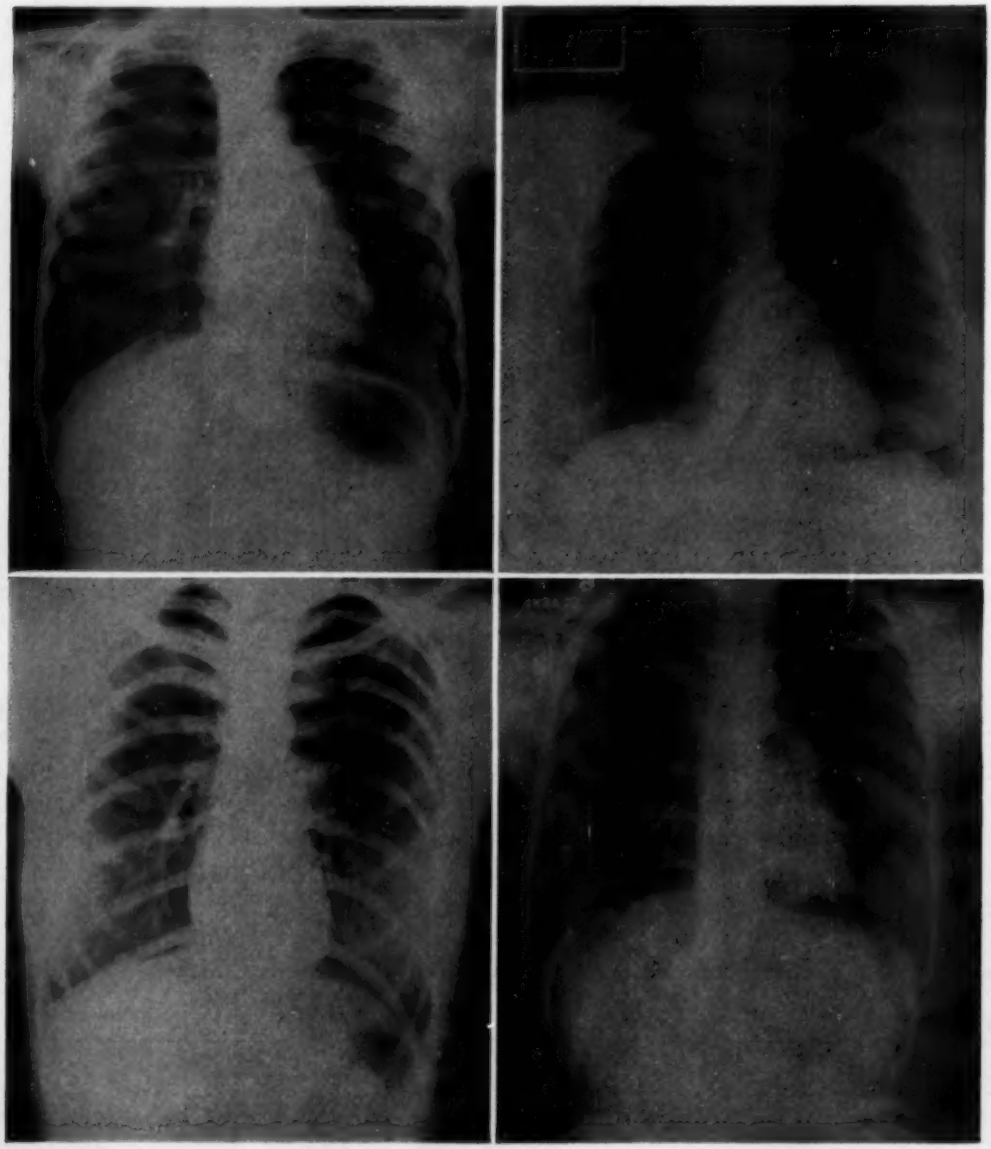

Fig. 3*A*.—Top row: two normal individuals. Bottom row: Ventricular septal defect (left) and patent ductus arteriosus (right).

3. *Combined Methods.*—Fig. 4 compares the detection rate by various methods, techniques, and combinations thereof. The efforts to improve the detection rate with x-ray by interpreting the contour of the heart in the absence of

cardiac enlargement raised the rate of detection of disease appreciably, but increased the number of false positives threefold when the same criteria were applied to the control group (columns 3 and 4). This figure also illustrates that the electrocardiogram detected more cardiacs than C/T ratio alone, and with only a slight increase in false positives (columns 3 and 5). Although electrocardiography detected slightly fewer cardiacs than C/T ratio plus contour readings, the number of false positives was only half that of this x-ray technique (columns

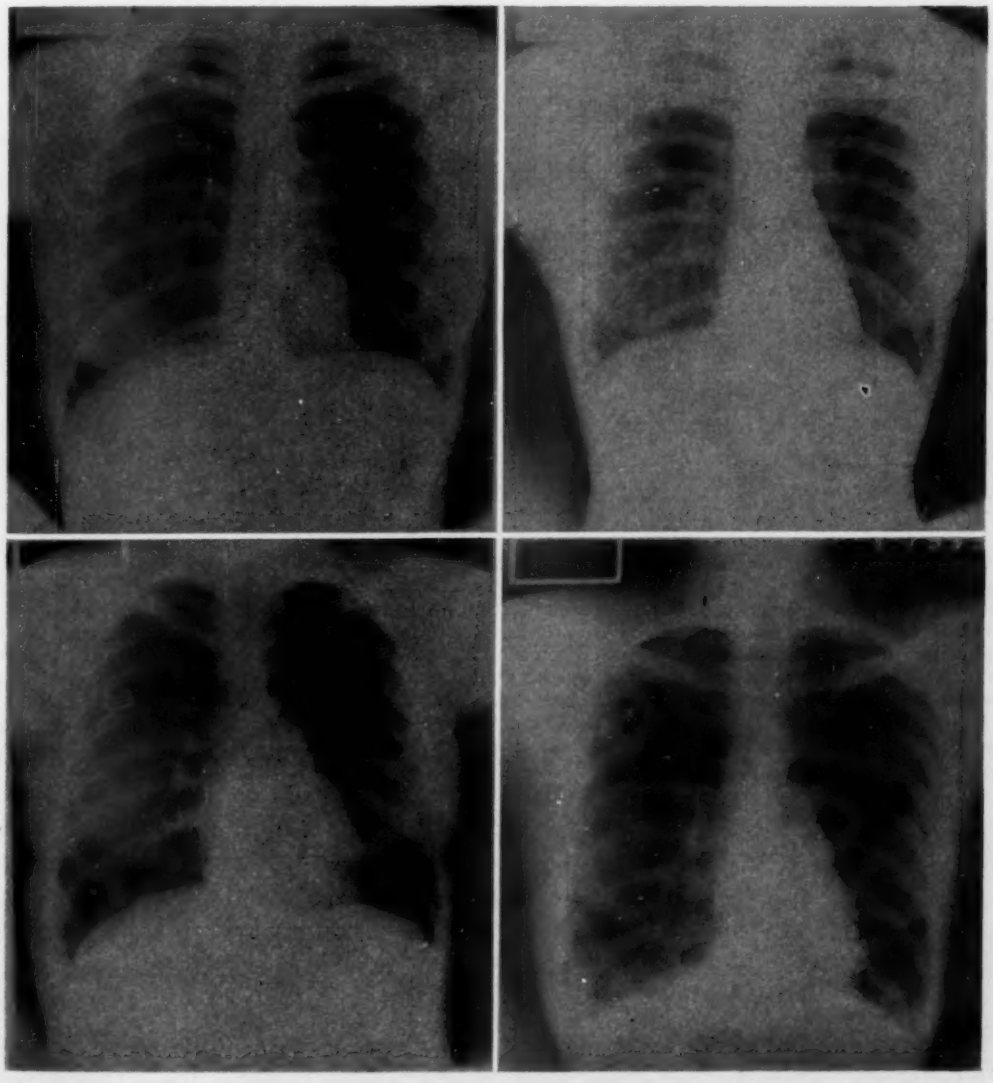

Fig. 3*B*.—Top row: two normals. Bottom row: Normal (left) and mitral stenosis (right).

4 and 5). The combination of ECG and C/T ratio was as good as contour reading plus C/T ratio, and had significantly fewer false positives (columns 4 and 6). The combination of C/T ratio, contour reading, and electrocardiography gave the best detection rate (92 per cent), but an extremely high number (29 per cent) of false positives (column 7).

Table III lists the cardiacs with normal ECG's and x-rays (C/T ratio and contour). There are slightly fewer cases with normal x-rays, but it must be remembered that the false positive percentage by these x-ray criteria is twice that of the electrocardiographic method.

COMPARISON OF DETECTION RATE WITH FALSE POSITIVES, X-RAY, AND ECG

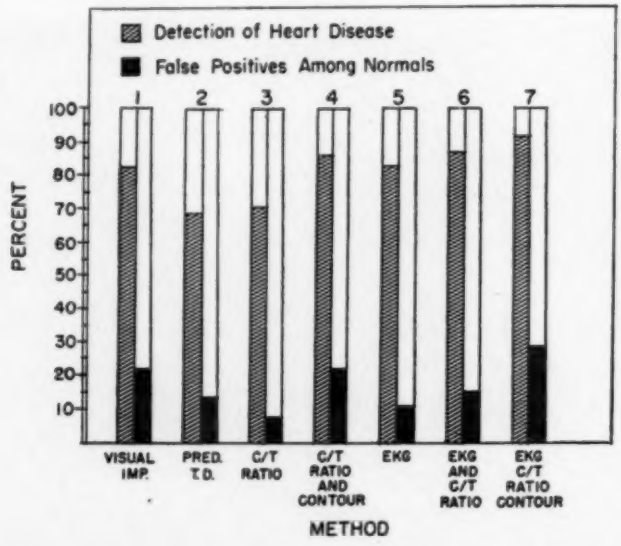

Fig. 4.—Comparison of detection rate with false positives, x-ray, and ECG. Results of applying various x-ray and ECG techniques of interpretation and combinations thereof to 218 cases. All results are in percentages. In each column, disease detection rates are on the left, false positives by the same technique on the right. Column 1 ("visual impression") includes all cases in which either cardiac enlargement or contour abnormality was suspected by the inspection of the x-ray. Transverse diameters over 10 per cent above those predicted by the Ungerleider-Clark tables are in column 2. Column 3 lists abnormal cardiothoracic ratios. Column 4 contains all cases who had either an abnormal C/T ratio or "abnormal" silhouette without cardiac enlargement. Columns 6 and 7 contain all cases with an abnormality in any of the modalities listed beneath them.

TABLE III. CARDIACS WITH COMPLETELY NORMAL X-RAY AND ECG

DIAGNOSIS	X-RAY	ECG	BOTH
Arteriosclerotic	0	2	0
Rheumatic	5	4	3
Congenital	7	7	4*
Hypertensive	3	4	1
Miscellaneous	3	5	2†
Total	18	22	10

*3 ventricular septal defects, 1 anomaly of aortic valve.

†2 cor pulmonale due to emphysema. Heart shadows normal, but emphysema evident. Both in congestive failure.

DISCUSSION

It is probable that the relatively high yield by all methods of survey was due in part to the manner of selecting patients. Each had disease (not necessarily cardiovascular) severe enough to cause him to seek the advice of a physician. The severity of heart disease in the present series was, therefore, probably greater in general than the cases detected in mass surveys for the first time. This difficulty, however seems unavoidable in comparing survey methods where known cardiacs must be used. Different detection rates would undoubtedly appear with a different selection of cases. For example, only 25 to 50 per cent of cases of angina pectoris without infarction may show electrocardiographic abnormality at rest;[20-22] it is not clear, however, what per cent have normal x-rays, or both normal x-rays and ECG's.[2,21,23,24] A study of this sort does not answer the question of how many previously unknown cardiacs could be detected by either method. Interestingly enough, however, several asymptomatic cases were detected in the attempt to collect 100 normal controls.

The effectiveness of "visual impression" when compared to x-ray measurement in detecting heart disease was somewhat surprising. Its success depends principally on correctly surmising cardiac enlargement (Table II), and this is undoubtedly based on an estimate of relative areas of the heart and thoracic cage. If the interpreter has had experience, a good correlation between actual and estimated measurements would be expected. The fairly large number of considerably enlarged hearts in the series would also support the correlation, because, in such cases, measurement would be superfluous. We feel, nevertheless, that measurement of the C/T ratio in borderline cases is helpful, and since little skill is required, the more helpful it will be to the less experienced interpreter.

Although in general the C/T ratio seemed preferable to prediction tables for cardiac transverse diameter, it is worth noting that when the thoracic cage is distorted, such is not the case. Both examples of cor pulmonale due to emphysema in this series revealed cardiomegaly only when these tables were used (Table III). Furthermore, in this comparison, it was necessary to favor the cardiothoracic ratio since no well established upper limits of normal for this method have been published. The best separation of cardiacs and controls in the present series was therefore used to determine this point.

False positives by x-ray and ECG methods rarely occurred in the same cases and a combination of the two, therefore, sharply increased the number of false positives. Since abnormalities by both methods also tended to occur in the same cases among known cardiacs, the detection rate was only moderately increased when the combined method was used. The ECG in a sense serves as a substitute for interpretation of cardiac contours without cardiac enlargement, since it detects many of the same cases (columns 1,3,5,6, Fig. 4).

Differences in false positives and detection rates of the seven methods of interpretation of x-rays and ECG's in Fig. 4 were analyzed statistically at the significance level of two standard errors separation; method 6 is superior to method 7 on basis of false positives and to methods 2 and 3 on basis of detection rate, but the present samples do not allow a distinction in detection rates be-

tween 6 and 1,4,5. Method 5, however, eliminates the x-ray and consequently most cases of noncardiac chest disease. Methods 1 and 4 require contour interpretation of the cardiac silhouette and, therefore, experienced roentgenologists. One would conclude from these samples, therefore, that for a survey for heart disease alone, method 5 (ECG alone) would be superior to any x-ray method whether the x-rays were "over-read" as in this study, with significantly higher number of false positives, or "under-read" as in other studies, with a significantly lower detection rate. On the other hand, if a combined heart-lung survey was to be done, method 6 (ECG and cardiothoracic ratio) would be the most practical approach.

The number of cases in each diagnostic category is too small to permit far-reaching conclusions, but the relatively low detection rates for both methods in the congenital group (Table III) may indicate that in surveys of school children, neither of these methods may be very reliable. This too, however, would depend on what types of congenital heart disease are included in the group surveyed. Congenital heart disease would, of course, not be much of a problem in an industrial survey.

SUMMARY AND CONCLUSIONS

1. The mass survey photoroentgenogram and a 4-lead electrocardiogram was applied to a group of 126 cases of known heart disease and ninety-two people without cardiovascular involvement.

2. In the interpretation of the borderline x-rays, mensuration was thought to be superior to inspection because of its objectivity. The cardiothoracic ratio when the internal diameter of the chest was measured at the level of the fourth anterior intercostal space, seemed to be at least as valuable a method of determining cardiac enlargement as the widely accepted Ungerleider and Clark tables for the prediction of transverse diameter. It has the added advantage that it is not necessary to know the height and weight of the individual. The lack of skill and experience required commend its use.

3. In view of the wide variability in the left cardiac border among normal people, interpretation of the contour of the heart in the absence of definite enlargement was hazardous and disproportionately increased the number of false positive readings.

4. When various methods and combinations thereof were used in the interpretation of the x-rays and the ECG's, there was, in general, a direct relationship between the efficiency of case detection and the number of false positives noted in the control group. The ranges are exemplified by the cardiothoracic ratio with a detection rate of 71 per cent and 8 per cent false positives, and a combined technique of cardiothoracic ratio, contour reading of the x-ray, and ECG, with a detection rate of 92 per cent and 29 per cent false positives.

5. The 4-lead electrocardiogram (I, aV_F, anterior and lateral V leads) detected a satisfactory number (83 per cent) of cardiacs, but had a false positive rate of 11 per cent. The reclassification of minor electrocardiographic abnormalities, however, caused an appalling fall in the detection rate, since these abnormalities occurred frequently among cardiopathies and were often the only sign of disease.

6. If the cardiothoracic ratio is combined with the 4-lead ECG described, the misleading left cardiac border of the heart with normal transverse diameter may be ignored. Detection rate is greater than either alone (87 per cent) and false positives are at a relatively modest figure (16 per cent). The scope of the mass survey will, of course, be increased by the addition of the x-ray since some cases of noncardiac chest disease will be detected. The ECG would, however, appear most practical for a survey limited to heart disease.

SUMMARIO IN INTERLINGUA

Cento vinti-sex casos cardiac (con juste representation de varie typos etiologic) e 92 subjectos normal esseva subjicite a un "inspection in massa" per medio de photoroentgenographia (a placas de 4 super 5 pollices) e per medio de un systema electrocardiographic a quatro derivationes. Le roentgenogrammas esseva legite separatemente per impression visual, determination del predicite diametro transverse (secundo le tabulas de Ungerleider e Clark), e computation del proportion cardio-thoracic in que le interne diametro thoracic esseva mesurate al quarte spatio antero-intercostal. Iste technica pro obtener le proportion cardio-thoracic pareva plus digne de confidentia que le technica usual. Su resultatos se conformava ben al valores del tabulas de predicite diametros transverse. Le technica require pauc dexteritate e non involve valores pro peso o altor. "Errores de excesso" in le examine del contornos roentgenographic in casos con normal diametros transverse resultava in un alte procentage de false interpretationes positive. Nos concludeva que le electrocardiogramma esseva melior como methodo unic, sed le procentage del correcte identificationes positive esseva meliorabile per adder le roentgenogramma e mesurar in illo solmente le proportion cardio-thoracic. Le electrocardiogramma servi como recimplaciamento del incerte processo de interpretar le silhouette cardiac in casos sin augmento del diametro transverse.

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AN ELECTROCARDIOGRAPHIC TECHNIQUE FOR MASS SURVEYS

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AUGUSTA, GEORGIA

THE possibilities of the electrocardiogram as a mass survey method have yet to be fully explored. The multiple lead system in current use for diagnosis is too time-consuming and requires too much technical skill to hold much promise for such a purpose. On the other hand, the 12-lead electrocardiogram is said to be the best single method of case finding, giving a higher detection rate than x-ray or questionnaire methods.[1] The technique herein described has been used successfully in a large survey,[2] and seems to retain the value of the 12-lead method while permitting the testing of as many as forty persons per hour.

METHOD

To study electrical events manifest in the frontal plane of the body, Leads I and aV_F were used, forming a biaxial reference system (Fig. 1). A Wilson type precordial lead with the exploring electrode in the midsternum at the level of the fourth intercostal space was added in order to sample forces predominantly from the right ventricle ("V anterior"). For the left ventricle, a midaxillary electrode at the same level was used because of the speed with which the position could be located, and the reproducability of its placement ("V lateral"). Both tracings are similar to those from the familiar, and diagnostically most important, precordial positions (V_1 and V_2, V_5 and V_6).

The steps in taking electrocardiograms were accelerated remarkably by several innovations: Electrode jelly was eliminated in favor of briskly wiping the skin 3 to 4 times with a 2 x 2 inch gauze square moistened with 60 per cent alcohol. This was left in place and the electrode placed upon it. Neither patient nor electrode require cleaning, as the alcohol quickly evaporates. In spite of the warnings of the manuracturers of electrode jelly, the alcohol substitute (which is not new) has been as good as the paste for the present purposes; no diagnostic errors have been traced to its use. Jelly is only used when the electrocardiograph must be attached for long periods, e.g., during cardiac catheterization or surgery. The usual strap limb electrode was abandoned for a newly designed snap-on type semi-permanently attached to short lead wires fixed to the examining couch at the point where the corresponding extremity will lie. Fig.

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2 illustrates such an electrode in place. The two precordial leads described above are more rapidly placed than those at different intercostal spaces. A handheld electrode has been the most satisfactory for this purpose. A steady flow of properly undressed patients can be supplied the technician by nontechnical personnel who also clip and label records.

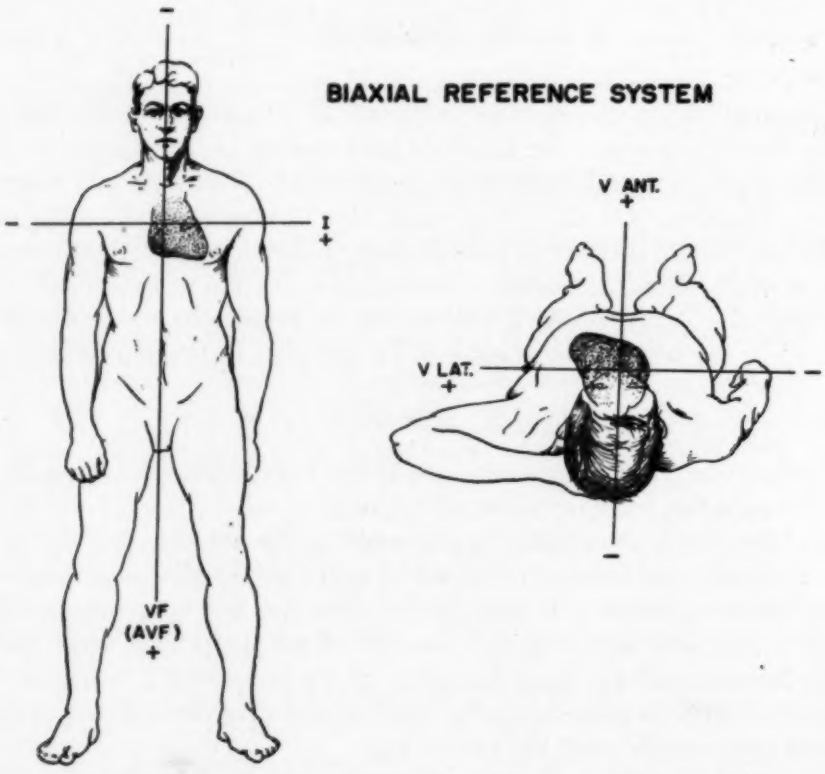

Fig. 1.—On the left is diagrammed the recording axes of Leads I and aV_F in the frontal plane of the body. Theoretically any electrical forces acting in the frontal plane must be manifest on one or the other of these two leads. On the right, a biaxial reference system in the transverse plane is made up of two precordial leads, as described in the text.

MATERIAL

In order to compare 3-, 4-, and 12-lead techniques, fifty individuals between 14 and 63 years of age who, on examination, gave no evidence of heart disease were selected from hospital personnel and the wards. Twenty-nine were men and twenty-one were women. These were used to establish normal criteria for "V anterior" and "V lateral" used in the studies below. One hundred patients with cardiovascular disease, each of whom had been thoroughly studied as an in-patient, were selected for the pathologic material. Ventricular enlargement was confirmed by autopsy (thirteen cases) or x-ray. Selection was made in the majority because the patient presented electrocardiographic evidence of heart disease, but other patients were selected without previous knowledge of their

electrocardiograms because they presented definite evidence of minimal degrees of cardiac enlargment. The figures, therefore, do not represent the diagnostic accuracy of either the 3-, 4-, or 12-lead electrocardiograms in an unselected series of cardiac patients. The accuracy of the systems may be compared with each other, however, and the interpretation of each system individually compared with the established diagnosis.

As a separate test of a similar 4-lead system, one hundred arrhythmias were selected at random from the electrocardiograph files by the technician, and were interpreted using only Lead I, aV_F, V_1, and V_5.

Fig. 2.—A "cuff" of a polysterene plastic* is tipped with a stainless steel electrode and the lead wire is attached by a small battery clip. This plastic has sufficient elasticity to hold it firmly on the extremity. Skin is prepared by wiping briskly with the small gauze pledget dampened with alcohol. This is left in place during the recording.

***Supplied by the Dow Chemical Company, Midland, Mich.**

Table I summarizes the criteria found to be most useful in the diagnosis of right, left, and combined ventricular hypertrophy. The measurements for the 12-lead system in establishing right and left ventricular hypertrophy are from the criteria of Sokolow and Lyon[3,4] and for combined hypertrophy, from the work of Goodwin and Pagnoni.[5] For combined hypertrophy in chronic rheumatic heart disease, the criteria of Rosenman and associates were applied.[6] The meas-

urements for the 3- and 4-lead adaptations of their methods were from the fifty normal subjects, omitting four of the five cases who had "abnormal" tracings without heart disease.

TABLE I

	CRITERIA FOR DIAGNOSIS OF VENTRICULAR HYPERTROPHY	
	12-LEAD	3- AND 4-LEAD ADAPTATION
Left	1. R_{V5} or $R_{V6} > 26$ mm. 2. R_{V5} plus $S_{V1} > 35$ mm. 3. Ventricular activation $> .05$ sec. in V_5 or V_6 4. Left axis deviation plus $T_3 > T_1$ 5. R $aV_L > 11$ mm.	1. $R_{V\text{-lat.}} > 23$ mm. 2. $R_{V\text{-lat.}}$ plus $S_{V\text{-ant.}} > 33$ mm. R_1 plus $S_{V\text{-ant.}} > 29$ mm. (3-lead) $S_{V\text{-ant.}} > 27$ mm. (3-lead) 3. Ventricular activation $> .05$ sec. in V-lat. 4. Left axis deviation plus QRS-T angle $> 50°$
Right	1. $R/S_{V1} > 1.0$ 2. R_{V1} 7 mm. 3. R_{1V} plus $S_{V5} > 10.5$ mm. S_{V5} or $V_6 > 7$ mm. 4. Ventricular activation $V_1 > .03$ sec. and > ventricular activation in V_5 or V_6	1. $R/S_{V\text{-ant.}} > 1.0$ 2. $R_{V\text{-ant.}} > 8$ mm. 3. $R_{V\text{-ant.}}$ plus $S_{V\text{-lat.}} > 12$ mm. 4. Ventricular activation in V-ant. $> .03$ sec.
Combined	1. "Vertical heart" plus ECG signs of left ventricular hypertrophy plus "clockwise rotation" seen by R > Q in aV_R, s > R in V_5, inverted T in V_1 2. In chronic rheumatic heart disease, left ventricular hypertrophy plus clockwise rotation plus "electrical position other than horizontal or semi-horizontal" plus P mitrale or auricular fibrillation 3. Voltage changes of both right and left ventricular hypertrophy in precordial leads	1. Signs of left ventricular hypertrophy plus QRS axis of $> 60°$ ("highly suggestive") 2. If chronic rheumatic heart disease, require also P mitrale or auricular fibrillation in addition to the above 3. Voltage changes of both right and left ventricular hypertrophy in precordial leads

The five "abnormal" electrocardiograms from the group without heart disease included one complete right bundle branch block, one nonspecific T-wave abnormality, one "left ventricular hypertrophy" (slight voltage increase in the precordial leads), one incomplete right bundle branch block, and one Wolfe-Parkinson-White syndrome. The voltage measurements of the record with the T-wave abnormality fell within the limits established by the other forty-five cases. The 4-lead electrocardiograms in the remaining forty-five cases were considered to be "normal", and their measurements were used for comparison with the records from the 100 pathologic cases. The basis for calling any 4-lead electrocardiogram normal was the finding of normal voltage measurements, normal scalar patterns and ventricular activation times (intrinsicoid deflections), and an angle between the QRS and T axes in the frontal plane of less than 50°.[7] There was, of course, complete agreement between 12- and 4-lead systems in the forty-five cases, and also in the five "abnormal" cases.

Since, theoretically, a recording from only a vertical, horizontal, and sagittal electrocardiographic axis would be needed to describe the electrical field of the heart, an attempt was made to see what percentage of diagnoses could be made, using Lead I as a horizontal component, Lead aV_F as a vertical component, and Lead "V anterior" as the sagittal component. This necessitated further revision of the established criteria for the diagnosis of left ventricular hypertrophy. The R wave deflection of the scalar electrocardiogram whose axis might be utilized as a horizontal component, Lead I, was added to the S-wave deflection of the anteriorly placed V lead. The range of the voltage sums of R_1 plus S V anterior for the normals and isolated left ventricular hypertrophies is seen in Table I and Fig. 2.

RESULTS

Left Ventricular Hypertrophy.—There were forty-one cases of isolated left ventricular enlargement in the present series. Using the criteria of Sokolow and Lyon (Table I), this diagnosis was established in thirty cases with the advantages of 12 leads. Six additional cases were considered "misses", but did have left bundle branch block. One case had complete right bundle branch block. Four records were within normal limits. This tabulation of discrepancies between the electrocardiogram and the clinical diagnosis was the same for the 4-lead system, with the exception that an additional case with slight left ventricular enlargement had a normal 4-lead tracing. This close agreement (98 per cent) might be expected if one compares the 4- and 12-lead criteria. Since the 12-lead criteria depend on precordial leads taken in only two positions, namely one over the anterior chest (V_1) and another over the lateral chest (V_5 or V_6), it is not surprising that similar measurements from leads "V anterior" and "V lateral" should give rather similar results. There is, in fact, no reason that V_1 and V_5 alone should not give equally good results.

Fig. 3 is a graphic representation of the voltage sums, S V anterior plus R V lateral, comparing the normal and the cases of isolated left ventricular hypertrophy. This measurement was the most valuable of all the criteria for the definite establishment of left ventricular hypertrophy. There were no cases in this series in which left ventricular hypertrophy could be definitely diagnosed that did not have an increased voltage. It can be seen that a fairly sharp separation between the normal hearts and those with left ventricular hypertrophy occurred at 33 mm.; a total of over 33 mm. was, therefore, required to make the diagnosis.

Right Ventricular Hypertrophy.—Of the twenty-one proved cases of isolated right ventricular hypertrophy, fourteen were diagnosed with the aid of 12 leads and the criteria established by Sokolow and Lyons. The most important of these was the finding of an R wave in Lead V_1 of over 7 mm., or an R to S ratio in V_1 greater than 1. Of the seven cases "missed", two were read as normal, two more appeared normal except for the finding of P mitrale, and three showed an RS R′ in V_1, without significant prolongation of the QRS indicative of incomplete right bundle branch block.[8] The criteria of the 4-lead diagnosis was essentially the same, modified for "V anterior" and "V lateral" (Table I). The

upper limits of RV anterior was 8 mm.; therefore, 9 mm. or more was considered as indicative of right ventricular hypertrophy. None of the normal subjects had an R to S ratio in "V anterior" greater than 1. It must be emphasized that all normal subjects were adults, and the above criteria would not be valid for children.[12]

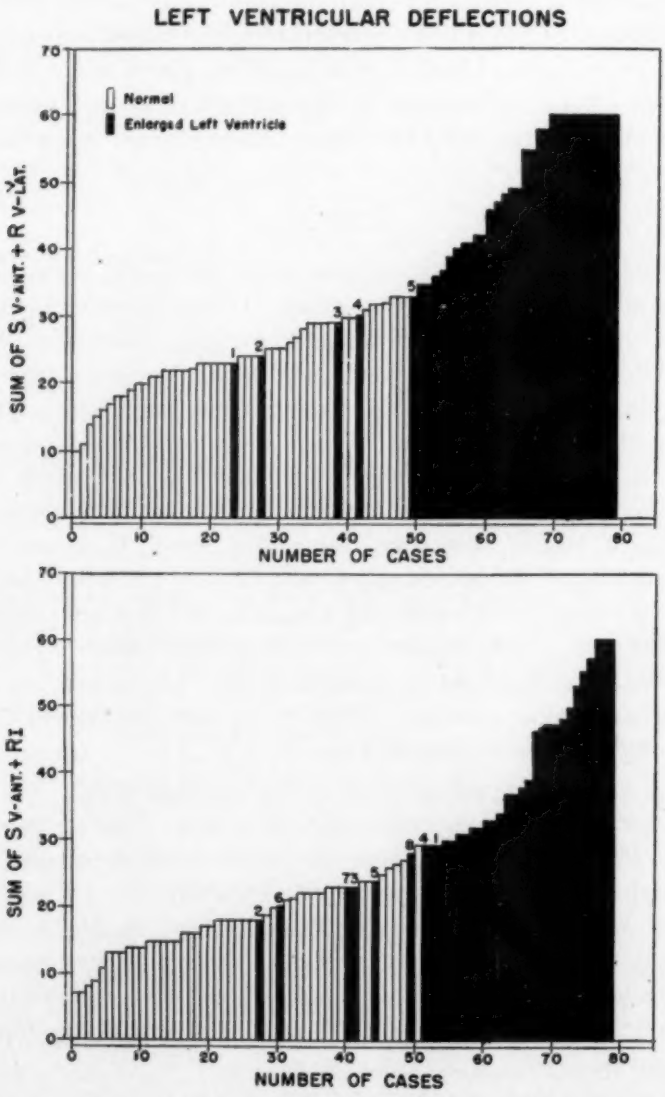

Fig. 3.—Plot of voltage measurements, as described in the text, of cases without heart disease and with isolated left ventricular enlargement. The numbered cases on both charts refer to the same patients. It can be seen that the cardiacs missed by the criteria of the top chart are also doubtful, or missed by that of the bottom. Cases 6 to 8 are also missed by the latter criteria.

It can be observed in Table II that the 4-lead had a slightly higher percentage of correct diagnoses than the 12-lead system. In one of these two cases, there was an RS R′ pattern in V_1 which was not present in "V anterior", but the latter lead revealed an R to S ratio greater than 1. By the criteria adopted

for this comparison, therefore, the 4-lead diagnosis would have been right ventricular hypertrophy, and the 12-lead "incomplete right bundle branch block." The latter pattern is, of course, often seen in right ventricular hypertrophy, and is usually considered "highly suggestive". Since it may be seen in other conditions, however, it was considered a "miss" for the purpose of tabulation. The other case showed an R to S ratio slightly greater than 1 in "V anterior" and somewhat less than 1 in V_1. One cannot claim that 4 leads are necessarily better than 12 in the diagnosis of right ventricular hypertrophy, for as long as certain diagnostic criteria are strictly adhered to, there will undoubtedly be discrepancies, even between two very similar systems, e.g., slight differences in electrode placement on different days will sometimes throw a mild abnormality into the normal group, or vice versa. There was actually an 86 per cent agreement in the electrocardiographic diagnosis among these twenty-one cases.

Combined Hypertrophy.—There were twenty-seven cases that showed either autopsy or clinical evidence of both right and left ventricular hypertrophy. Authorities agree that this diagnosis is very difficult electrocardiographically, as only about 25 per cent can be definitely diagnosed.[5,6] The criteria used are listed in Table I.

In the patients in our series who had chronic rheumatic heart disease, the criteria of Rosenman and associates were used. By defining the terms, "horizontal or semihorizontal," one concludes that this means an axis deviation of the mean QRS vector of less than plus 60°.[9] The translation of these scalar pattern criteria into vector terms should enable one to make the diagnosis with 2 leads in the frontal plane and the 2 leads in the transverse plane.

Using these criteria with 12 leads, only 11 of 27 were correctly diagnosed, 6 of the "misses" showed left ventricular hypertrophy, 3 demonstrated complete right bundle branch block, 2 had incomplete right bundle branch block, 1 right ventricular hypertrophy, 1 complete left bundle branch block, 1 was "highly suggestive" because of the combination of a "vertical heart", and left ventricular hypertrophy, 1 was normal except for P mitrale, and 1 showed nonspecific T-wave changes. Using 4 leads, the diagnosis was also made in 11, but not exactly the same cases. There was, therefore, only an 89 per cent agreement between the 4- and 12-lead electrocardiographic diagnoses. The "misses" by the 4-lead system showed 6 left ventricular hypertrophies, 3 complete right bundle branch blocks, 2 incomplete right bundle branch blocks, 1 right ventricular hypertrophy, 1 complete left bundle branch block, 1 "suggestive" combined hypertrophy, and 2 nonspecific T-wave changes.

Myocardial Infarction.—There were eight cases studied within two weeks of the initial pain. All cases had substantiating clinical evidence of myocardial infarction. The diagnostic pattern of wide, deep Q wave, and elevated S-T segment was found in at least one of the 4- leads used, as well as in the 12-lead system in seven cases. The remaining case showed complete left bundle branch block, and a greatly elevated S-T segment over the anterior chest. There was, therefore, 100 per cent agreement in this small group. There were three old infarctions well substantiated historically, and these were diagnosed either by

TABLE II

CLINICAL DIAGNOSIS	NO. CASES	12-LEAD CORRECT	4-LEAD CORRECT	3-LEAD CORRECT	4-LEAD AGREES WITH 12-LEAD	3-LEAD AGREES WITH 12-LEAD
Normal	50	45 (90%)	45 (90%)	45 (90%)	50 (100%)	50 (100%)
Left ventricular hypertrophy	41	30 (73%)	29 (71%)	28 (68%)	40 (98%)	39 (95%)
Right ventricular hypertrophy	21	14 (67%)	16 (76%)	16 (76%)	18 (86%)	18 (86%)
Combined hypertrophy	27	11 (41%)	11 (41%)	3 (11%)	24 (89%)	17 (63%)
Myocardial infarction—old	3	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)
Myocardial infarction—recent	8	7 (88%)	7 (88%)	7 (88%)	8 (100%)	8 (100%)
Total	150	110 (73%)	111 (74%)	102 (68%)	143 (95%)	135 (90%)
ELECTROCARDIOGRAPHIC DIAGNOSES						
Complete RBBB	7	5 (100%)	5 (100%)	5 (100%)	5 (100%)	5 (100%)
Incomplete RBBB		6 (86%)	6 (86%)	6 (86%)	5 (71%)	5 (71%)
Complete LBBB		8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)
WPW		1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)
Nonspecific T wave		3 (100%)	2 (67%)	2 (67%)	2 (67%)	2 (67%)
Auricular fibrillation		7 (100%)	7 (100%)	7 (100%)	7 (100%)	7 (100%)
Complete heart block		1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)

the absence of R waves in the anterior chest lead, without evidence of left ventricular hypertrophy or left bundle branch block, to explain a Q wave in this location,[9,10] or a "diagnostic" Q wave in one of the frontal plane leads.[9] In this group of eleven electrocardiograms, there was, therefore, 100 per cent agreement between the 12- and 4-lead systems.

Diagnoses Supported Only by the Electrocardiogram.—Seven complete right bundle branch blocks and nine complete left bundle branch blocks were equally well diagnosed by 4 or 12 leads. There was, therefore, 100 per cent agreement in these sixteen cases. For the 4-lead diagnoses, the only criteria used were the proper prolongation of the QRS complex, and the assumption that the terminal 0.04 second vector pointed towards the blocked ventricle.[7] In the seven cases of incomplete right bundle branch block, the single criteria used was the RS R′ complex in Lead V_1 or "V anterior" respectively. Prolongation of the QRS was not demanded.[8,10] In one case, this pattern showed up in V_1, but not in "V anterior" and in the other cases, the opposite was true. There was, therefore, agreement in five out of seven cases. One case showed the Wolfe-Parkinson-White picture, and three cases showed nonspecific T-wave changes in the 12-lead electrocardiogram. There was agreement in all except one of the latter; the QRS-T angle was only 45°, the upper limit of normal, as judged by the bipolar plot in the frontal plane. Since the 12-lead electrocardiogram and the 4-lead electrocardiogram were taken several hours apart, it is possible that the QRS-T angle had actually changed during this interval in an otherwise normal patient. Seven instances of auricular fibrillation and one complete heart block also were detected by 4- and 12-lead systems.

Arrhythmias.—This test was approached with confidence because of the frequency with which auricular activity is most readily evident in V_1 or V_2, and because of the ease with which arrhythmias had been detected in the previous 150 electrocardiograms (Table II). When the readings were compared with those from the 12-lead tracings, the agreement was almost perfect. The two cases of nonagreement were due to a shifting origin of the impulse which resulted in different rhythms being present in different leads, which were, of course, taken consecutively, and not simultaneously. The ease of interpretation appeared to be more dependent on the technical perfection and the length of the record than on the variety of leads. The distribution of diagnoses is listed in Table III.

Interpretations Based on 3 Leads.—The diagnosis of left ventricular hypertrophy was made when the sum of the R wave in Lead I and the S wave in "V anterior" in the unknown tracing exceeded the normal figure (Table I), or when the S wave in "V anterior" of the unknown tracing exceeded normal limits. Two cases with voltage changes of left ventricular hypertrophy by the 12-lead system, and who actually had a minor degree of cardiac enlargement due to essential hypertension, were called normal by 3-lead criteria. The results of this attempt at establishing criteria for a system of 3-lead electrocardiography in the diagnosis of left ventricular hypertrophy are seen in Fig. 2.

Since the anteriorly placed V leads are so important in the diagnosis of right ventricular hypertrophy, it would be expected that if such a lead were present, most of the diagnoses of right ventricular hypertrophy could be made, and this

TABLE III

12-LEAD DIAGNOSIS	NO. CASES	4-LEAD CORRECT
Sinus arrhythmia	8	8 (100%)
Sinus bradycardia	10	10 (100%)
Shifting pacemaker	1	1 (100%)
First degree heart block	16	16 (100%)
Second degree heart block	4	3 (75%)
Complete heart block	13	13 (100%)
Wenkebach's phenomenon	2	2 (100%)
Pulsus bigemini	3	3 (100%)
Ventricular tachycardia	4	4 (100%)
Supraventricular tachycardia	8	7 (88%)

was found to be true. There was a discrepancy between 3- and 12-lead diagnosis in only three cases, and between 3- and 4-lead diagnosis in none.

There was disagreement between the 3- and 12-lead electrocardiographic readings in 15 of 150 tracings (10 per cent). Ten of these 15 had a clinical diagnosis of combined hypertrophy. By the 3-lead system, 4 were labeled as normal, 3 as left ventricular hypertrophy, 1 as incomplete right bundle branch block, and 2 as right ventricular hypertrophy.

Of the 96 abnormal 12-lead tracings, 7 were called normal when only 3 leads were available. As a screening method, therefore, the 3-lead system would have missed only 7 out of 96 cardiacs (7 per cent) that would have been detected if 12 leads had been taken. "P mitrale" was apparent in 3 of these. Of the 7 patients called "normal" by 3-leads, the 12-lead tracings showed 1 right ventricular hypertrophy, 4 combined hypertrophy, and 2 left ventricular hypertrophy. A detailed comparison of the accuracy of the 3-lead system when compared with the clinical and 12-lead diagnoses is found in Table II.

DISCUSSION

Table II summarizes the results. Using the previously outlined criteria, there seems to be little difference between the 12- and 4-lead systems, but some decrease in accuracy with only 3 leads.

Extensive further experience with the 4-lead system as a survey method while this paper was being prepared suggests, as expected, that the number of normals used as a control for the diagnostic criteria in this study is inadequate. An individual with an apparently normal cardiovascular system occasionally has a "left ventricular potential" slightly higher than the upper limits of normal as here defined. Some of these cases also have, by voltage criteria, an abnormal 12-lead electrocardiogram. The same has rarely been found also in the case of

"right ventricular potentials"; most of the latter have involved an unusual shift of the transitional zone to the right, and are sometimes associated with thoracic deformity. The "normal" range indicated here must, therefore, be regarded as tentative.

The number of myocardial infarctions represented in this series is small, and it appears certain that in a larger series, there would be a few cases missed on the 4-lead system that might be apparent if more precordial leads were available.[11] This probably applies more particularly to the isolated findings of absent R waves over some of the precordial leads in the presence of an old infarction; on the other hand, it seems unlikely that in the presence of acute myocardial infarction with S-T and T wave changes, that the latter could be missed on all four of the leads used.

CONCLUSIONS

1. A rapid technique for obtaining two limb and two precordial leads is described. The speed depends principally upon the use of special snap-on limb electrodes and the elimination of electrode jelly.
2. Detailed criteria for analyzing these tracings is presented.
3. The difference in diagnostic accuracy between the routine 12-lead electrocardiographic system, and a 4-lead system, composed of Leads I, aV_F, and an anterior and lateral V lead, was negligible in a selected series of fifty normal subjects and 100 cardiac patients. Discrepancies in diagnosis did not always favor the 12-lead electrocardiogram.
4. A similar 4-lead system consisting of V_1, V_5, I, and aV_F seemed to be equally as good as 12-leads in the diagnosis of 100 unselected arrhythmias.
5. A 3-lead system, I, aV_F, and V anterior, showed 10 per cent disagreement with the specific 12-lead diagnosis, but failed to identify as abnormal only 7 per cent of ninety-six abnormal electrocardiograms in the same series.
6. The 3- or 4-lead electrocardiogram secured and interpreted as outlined appears to have a useful place in cardiac surveys.

SUMMARIO IN INTERLINGUA

Le plus alte procentage de identification positive de morbo cardiac in examines in massa es apparentemente obtenite per medio del electrocardiogramma a 12 derivationes. Sed iste methodo es lente, lo que limita su utilitate. Le grande majoritate del diagnoses electrocardiographic es basate super le áxes de plano frontal de importante componentes, le relation de complexos auricular e ventricular, e mesuramentos ab derivationes placiate proxime al duo ventriculos. Un systema a quatro derivationes (I, aV_F, e V anterior e lateral) esseva comparate con le usual systema a 12 derivationes in 150 casos con firmemente establite diagnoses. Le criterios diagnostic usate in le duo casos esseva simile. Le differentias de exactitude esseva negligibile. Un simile systema a quatro derivationes (I, aV_F, V_1, e V_5) se monstrava similemente efficace in 100 non-selegite casos de arrhythmias. Le rapiditate del registration esseva grandemente accelerate per le substitution de tampons a alcohol pro le pasta electrodic e de

un porta-electrodo a forma de manchette plastic pro le electrodo conventional. Le resultatos indica que iste methodo permitte le accurate examine electrocardiographic de grande gruppos de subjectos con un rapiditate de 40 personas per hora.

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THE APPROXIMATE DETERMINATION OF LEAD VECTORS AND THE BURGER TRIANGLE IN NORMAL HUMAN SUBJECTS

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THE introduction of Burger's lead vector concept[1,2] into electrocardiographic theory has stimulated a number of attempts to establish accurately the quantitative relationships between the electromotive forces of the heart and the various leads of the electrocardiogram. The Burger group has studied these relationships rather extensively in a three-dimensional, nonhomogeneous model of the human body.[1,2] More recently, Frank, employing an electrically homogeneous three-dimensional model, confirmed and extended the scope of Burger's original observations.[3]

Attempts to establish similar relationships in the case of the living human body have been more limited in nature due to the relative inaccessability of the internal structures of the thorax. Wilson applied current dipoles to the anterior chest wall of human beings and determined the relationships between these dipoles and the conventional extremity leads of the electrocardiogram.[4] In discussing his observations Wilson recognized fully that the electrical field produced by a current dipole located on the precordium might differ considerably from that produced by the heart. Den Boer attempted to circumvent this objection by establishing current dipoles in the cardiac region of human cadavers.[5] This method is open to the objection that the conductivity of tissue may change after death. Also, for theoretical reasons which will be presented later, intracardiac determinations of lead vectors are not necessarily more precise and meaningful than determinations made in other ways.

On the basis of principles established during a study of two-dimensional models of the human body,[6] and through the application of recently acquired knowledge concerning the electrical properties of intrathoracic tissues,[7] we feel that it is possible to establish the relationships between the electromotive forces of the heart and the extremity leads with greater accuracy than has been previously reported. It is the purpose of this communication to report the results of such a study as performed on normal, human subjects.

The theoretical basis of the present study lies in the lead field concept. By definition the lead field is the electrical field produced in the body when a given set of lead connections is energized with current from an external electromotive

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force. The lead vector and the lead field are not mutually independent physical entities, for it has been demonstrated that the lead vector is identical to the potential gradient of the lead field produced by one unit of electrical current.[6] On this basis the mapping of the isopotential functions of a lead field provides a great deal of information concerning the physical characteristics of the lead connection, since the potential gradient of the field at any point is directed normally to the isopotential surface at that point, and the magnitude of the gradient is inversely proportional to the spacing which represents a given potential interval in the vicinity of the point.

METHODS AND MATERIALS

With the foregoing basic principles in mind, we produced square wave energization of the Einthoven lead pathways of six human subjects with 1 Ma. of direct current by means of a 45-volt battery in series with an electrical key and suitable resistor. The subjects were adult men who were all normal with the exception of one person who had diabetes mellitus which was adequately controlled with diet and insulin. The basic technique consisted of moving a disc-like exploring electrode, 5 mm. in diameter, over the torso until an electrocardiograph connected between it and a reference electrode on the chest failed to record a deflection when the key was closed during electrical diastole. In this manner the surface trace of an isopotential sheet of the lead field was mapped out with considerable precision, since shifting the exploring electrode as little as 0.5 mm. from the null position produced an observable deflection in the electrocardiographic tracing when the key was closed. The portion of the chest wall which included the entire cardiac region was mapped out at potential intervals of either 1 or 1.5 mv. The subjects were then photographed from the front and the back, and line copies of the photographs were superimposed in a manner which gave essentially a frontal projection of the surface isopotential traces in their entirety.

The direction and magnitude of the lead field gradient was determined at two arbitrary points on the chest wall. One of these points was located on the anterior chest wall directly overlying the approximate center of the ventricles. The other point was located on the posterior chest wall directly behind the anterior point. The direction of the gradient was determined by fitting a straight line tangent to the isopotential trace at a given point and then determining the angular direction of a straight line constructed perpendicular to the tangent line. Following this procedure, the potential difference in the lead field was measured between two points 5 cm. apart and located on the perpendicular line equidistantly from the point under investigation. One fifth of the potential difference thus determined was taken as the magnitude of the lead field gradient. The square waves recorded during this procedure exhibited a variable type of transient response. In some cases the onset and offset exhibited a slight degree of overshoot; in other cases a slight degree of undershooting was noted. In analyzing these records the transients were disregarded and only the distance between the base line and the steady portion of the deflections was measured.

Finally, we measured the potential difference which was produced between the anterior and posterior points when each of the lead pathways was energized with 1 Ma. of direct current. Dividing these potential differences by the distance between the two points gave an approximate value of the sagittal components of the lead field gradients. These sagittal components were employed in determining the angle of tilt of the lead vectors with respect to the anatomic frontal plane.

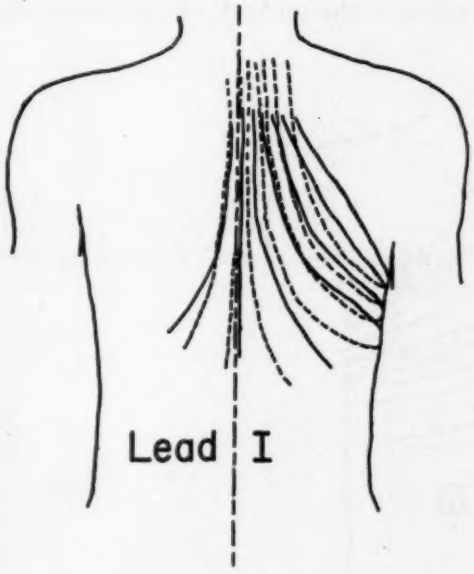

Fig. 1.

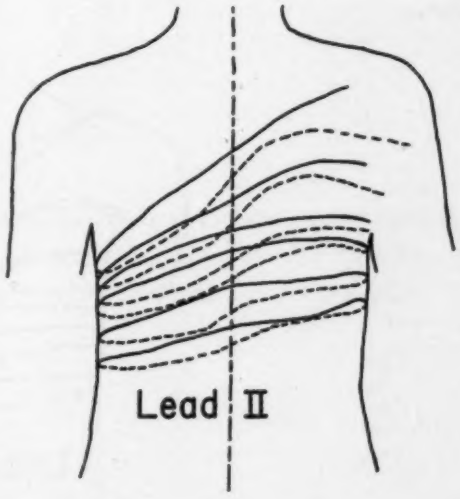

Fig. 2.

Fig. 1.—Typical Lead I field map of a normal human subject. Interval between isopotential lines = 1.0 mv.

Fig. 2.—Lead II field map. Same subject as Fig. 1. Interval between isopotential lines = 1.5 mv.

RESULTS

The ideal lead field as described by McFee and Johnston[8] and by ourselves[9] is one that is perfectly uniform. As will be seen later this ideal requires some elaboration and modification, but as originally proposed, the isopotential surfaces of the ideal lead field are plane and parallel, and the potential gradient of the field is invariant throughout. As a result of this uniformity, all of the electromotive forces of the heart are projected on the same axis of registration and recorded with the same weight by the associated electrocardiographic connection.

With this theoretically ideal situation in mind, we inspected the lead field maps of our subjects in order to determine how nearly they represented isopotential sheets which might be plane and parallel. In the case of Lead III (Fig. 3) the isopotential maps were rather uniform in the cardiac area. In the case of Lead II (Fig. 2) they were less uniform, and in the case of Lead I (Fig. 1) a considerable departure from plane-parallelism was observed. The conclusion

was drawn from these observations that the lead vectors associated with the Einthoven lead connections, especially with Lead I, varied in direction and magnitude throughout the cardiac region.

Due to this variability of the lead field patterns, our quantitative determinations were arbitrarily limited to the anterior and posterior points described above. In the case of each lead connection we computed a weighted mean which consisted of three-fourths of the anterior point gradient and one-fourth of the posterior point gradient. This weighted mean was taken as an approximation of the frontal plane component of the lead vector in the vicinity of the ventricular center.

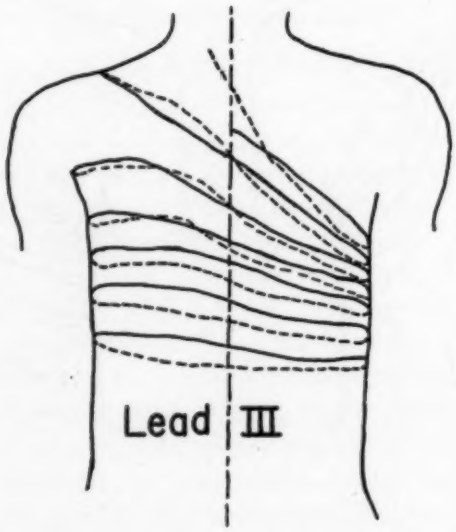

Fig. 3.—Lead III field map. Same subject as Fig. 1. Interval between isopotential lines = 1.5 mv.

In each of the six subjects the frontal plane components of the Lead I and Lead II vectors were plotted as arising from the same origin, and the frontal plane component of the Lead III vector was plotted as arising from the terminus of the Lead I vector. Theoretically such a plot should have resulted in a closed triangular configuration, but in practice such closure failed to occur. Because we had more confidence in the accuracy of our angular determinations than in our measurements of lead vector magnitudes, we adjusted our data only for errors in the latter. This was accomplished by computing a closed triangle whose sides had the same orientation as the sides of the open configuration, and the perimeter of which equalled the sum of the sides of the open configuration. These closed triangles were regarded as the frontal plane projections of the Burger triangles of the subjects. The difference between the adjusted and originally calculated values of magnitude was 10 per cent or less.

These magnitudes and directions are given in Tables I and II, respectively. The dimensions of the magnitudes are mv./cm./Ma. They range from 0.47 to 0.62 in the case of Lead I, from 0.56 to 0.70 in Lead II, and from 0.73 to 0.93 in Lead III. The directions range from −13 to −17 degrees in the case of Lead I,

from 62 to 75 degrees in Lead II, and from 110 to 117 degrees in Lead III. As a matter of interest, the direction of the Lead aV_F vectors was calculated because this lead is sometimes employed as the vertical connection in vectorcardiography. The range of directions of this lead vector was 88 to 99 degrees.

TABLE I. MAGNITUDES OF FRONTAL PLANE COMPONENTS OF THE LEAD VECTORS—mv./cm./Ma.

SUBJECT	LEAD I	LEAD II	LEAD III
J.H.	0.47	0.56	0.73
B.E.	0.62	0.56	0.80
J.C.	0.54	0.63	0.73
J.S.	0.62	0.70	0.93
D.B.	0.57	0.56	0.74
J.E.	0.56	0.66	0.79

TABLE II. ANGULAR DIRECTIONS OF FRONTAL PLANE COMPONENTS OF LEAD VECTORS—DEGREES

SUBJECT	LEAD I	LEAD II	LEAD III	LEAD aV_F
J.H.	−17	72	113	96
B.E.	−18	68	118	98
J.C.	−15	62	110	88
J.S.	−15	75	116	99
D.B.	−15	68	117	96
J.E.	−13	66	111	91

The ratio of the sagittal components of the lead field vectors to the adjusted frontal plane components was taken as the trigonometric tangent of the angle of tilt of the lead vectors with respect to the anatomic frontal plane. The values of angular tilt were given in Table III. A positive angular value indicates that the terminus of the lead vector is directed posterior to the frontal plane; a negative value indicates that it is directed anteriorly. In all cases the Lead I vector was directed posteriorly and the Lead III vector anteriorly. In the case of the Lead II vectors some were posterior and some anterior. In most cases the angles of tilt were so small that for practical purposes the Burger triangle was virtually coplanar with the anatomic frontal plane.

TABLE III. ANGLE OF TILT OF LEAD VECTORS WITH RESPECT TO ANATOMIC FRONTAL PLANE—DEGREES

SUBJECT	LEAD I	LEAD II	LEAD III
J.H.	8	−7	−11
B.E.	4	−14	−11
J.C.	11	4	−5
J.S.	5	1	−2
D.B.	2	−9	−8
J.E.	3	−4	−8

As has been pointed out in previous publications,[6,10] a set of Einthoven lead vectors may be employed to construct a triaxial frame of reference. Fig. 4 is such a triaxial system derived from the lead vectors of one of our subjects. The heart vector, H, is the manifest potential determined at the height of the R deflection in Lead II. The lead deflections are rounded off to the nearest 1/10 of a millivolt in this plot in order to show clearly that it satisfies Einthoven's law exactly, even though it is not derived from an equilateral triangle. A feature not present in previously published plots of this type is the addition of the circular coordinate plot for the purpose of indicating the magnitude of the manifest potentials. The dimensions of these circular coordinates are those of an electric current moment, i.e., milliampere-centimeters. It will be recalled that the dimensions

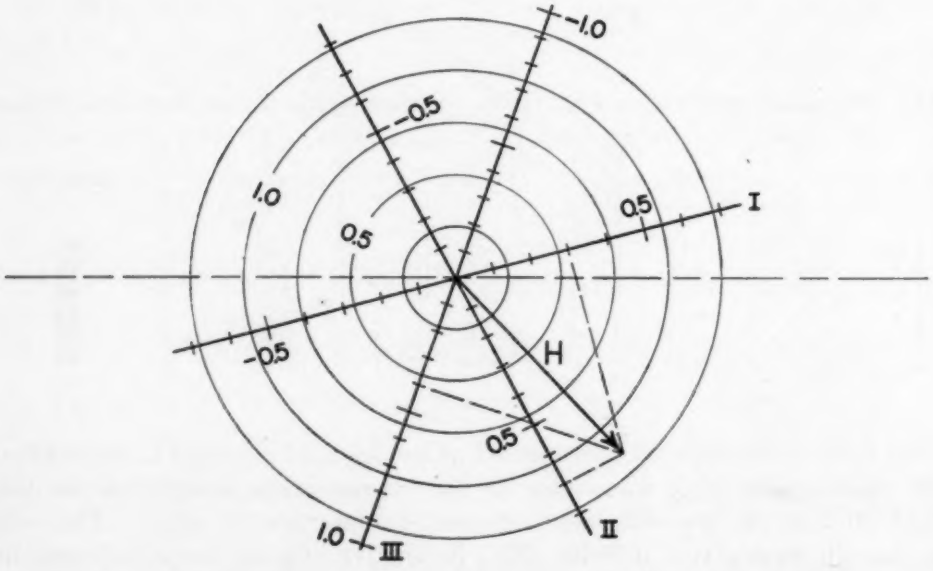

Fig. 4.—Triaxial electrocardiographic frame of reference constructed from the lead vectors of subject J. C. Discussion in text.

of the lead vector are mv./cm./Ma. Therefore the dimension of an electrocardiographic lead, which is the dot (or scalar) product of the two, is millivolts. Due to a theoretical development to be given later, which concerns distortion of lead fields by the intracardiac mass of blood, it seems unlikely that the circular coordinates of Fig. 4 possess a strict quantitative significance. However, the angular values shown in the plot probably represent a reasonably good first approximation of true angular values.

DISCUSSION

The method described here for determining lead vectors and Burger triangles in human subjects appears to be superior to those previously described. In employing living subjects we have avoided those errors due to possible changes

in the electrical conductivity of tissues after death. In employing posterior as well as anterior points on the chest wall for the determination of lead vectors we have probably improved on the efforts of Wilson[4] who employed anterior points only. Due to the relative inaccessability of interior points, it was necessary to employ some approximations in our calculations, but in general these approximations have seemed to us to be reasonably acceptable.

Apart from the quantitative determinations which we made, the mapping of the lead fields appears to have enhanced the value of this study. According to the principles outlined earlier, inspection of a lead field configuration provides a rather clear appreciation of lead vector variability throughout the cardiac region. The lead fields determined in this study, particularly the Lead I fields, failed to meet the condition of uniformity of the so-called ideal lead field. On the basis of experiments with a two-dimensional model of the human body, it seems likely that the technique described here may be used to test various types of synthetic leads for the purpose of devising leads which closely approximate the ideal situation.

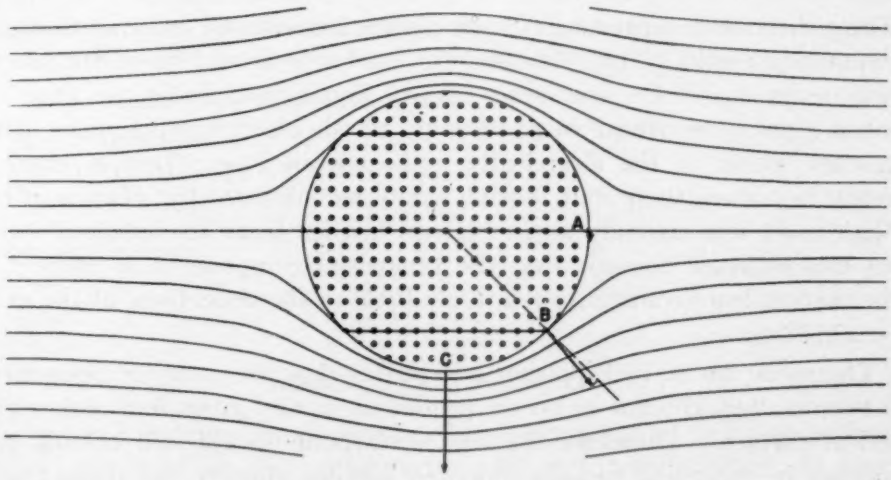

Fig. 5.—Distortion of an ideal lead field by the intracardiac mass of blood. The blood mass has been idealized as a spherical volume conductor whose conductivity is ten times that of the surrounding medium. Discussion in text.

Probably our greatest source of error in the determination of lead vectors arises from the fact that the intrathoracic tissues of the body are not electrically homogeneous. Frank[11] feels that electrical inhomogeneities remote from the heart have little effect upon the equivalent cardiac dipole, but that inhomogeneities in proximity to the heart, such as the intracardiac mass of blood, may exert a profound effect. We believe that essentially the same is true in regard to lead vectors, and have attempted on a limited theoretical basis to determine the nature and magnitude of the distortions due to the intracardiac blood mass.

Fig. 5 depicts the distortion of a lead field by a mass of blood which has been idealized into a spherical volume conductor having ten times the conductivity of the surrounding medium. The isopotential sheets in the figure were

plotted from the equations given in the appendix. This field becomes uniform in regions remote from the sphere and would therefore be an ideal lead field if the blood mass were not present.

An analysis of the figure and its equations reveals that the distorted lead field possesses some interesting and important properties. For instance, the potential gradient within the spherical blood mass proves to be invariant, and co-directional with the potential gradient of regions remote from the blood mass; but the magnitude of the gradient within the sphere is only one-fourth that which exists at distant points. On this basis it would appear that little or nothing is to be gained by determining extremity lead vectors from intracardiac measurement of lead fields as opposed to measurements made in regions relatively remote from the heart.

A somewhat paradoxical situation is the "short circuiting" effect upon current dipoles in the vicinity of the blood mass. One might anticipate a priori that the relatively high conductivity of the spherical mass would reduce the contribution of current dipoles to the electrocardiographic deflection. This appears to be true in the case of tangentially oriented dipoles, and Equation 4 indicates that the contribution of such dipoles located just external to the spherical boundary would be only one-fourth of what it would be in the electrically homogeneous case. On the other hand, Equation 3 indicates that radially oriented dipoles contribute more strongly to the electrocardiographic deflection than they would in the electrically homogeneous case. Just external to the spherical boundary their contribution would be enhanced by a factor of two and one-half, and less strongly so in regions farther from the spherical boundary. From this analysis it seems that the tangential components of current dipoles in the myocardium contribute relatively little to the deflections of the extremity electrocardiogram.

The term, sin θ, in Equation 3 indicates that the radial components of the lead vectors obey the law of vector projection at any given level external to the spherical surface. Therefore the lead connection would still exhibit vectorial properties in recording radially oriented dipoles, despite the distorting effects of the spherical blood mass. It is not certain that electrical sources and sinks in the ventricular myocardium are radially oriented, but it is probable that those which contribute most heavily to the extremity electrocardiogram are approximately so oriented.[12] On this basis it seems likely that certain lead connections, whose fields would approach the ideal form in an electrically homogeneous medium, will record the electromotive forces of the heart in at least a quasi-vectorial manner.

SUMMARY

1. The Einthoven lead connections of six human subjects were energized with square wave impulses of 1 Ma. of direct current, and the body surface traces of the lead fields were mapped.

2. Methods are described for calculating lead vectors and Burger triangles from the lead fields, and the data thus computed are given in tabular form.

3. The Lead III field approximates the ideal lead configuration. The Lead II field and especially the Lead I field deviate significantly from the ideal configuration.

4. A theoretical analysis of lead distortions due to the intracardiac mass of blood shows that tangential components of current dipoles in the myocardium contribute relatively little to the deflections of extremity electrocardiograms. Despite lead distortions due to intracavitary blood, the electromotive forces of the heart are probably recorded in a quasi-vectorial manner.

APPENDIX

Field equations from which Fig. 5 was plotted.
Field external to the sphere:

$$V_e = k[r - \frac{3}{4}\frac{R^3}{r^2}] \sin \theta \quad (1)$$

Field inside the sphere:

$$V_i = \frac{k}{4} r \sin \theta \quad (2)$$

Where k is a constant, R is the radius of the sphere, and r, θ are conventional polar coordinates with the sign of θ taken in the usual electrocardiographic sense.

The lead vector components of the external field are,

Radial component:

$$\frac{\delta V_e}{r} = k\,[1 + \frac{3}{2}\frac{R^3}{r^3}] \sin \theta \quad (3)$$

Tangential component:

$$\frac{1}{r}\frac{\delta V_e}{\delta \theta} = k\,[1 - \frac{3}{4}\frac{R^3}{r^3}] \cos \theta \quad (4)$$

SUMMARIO IN INTERLINGUA

1. In sex subjectos human le connexiones derivational de Einthoven esseva energisate per impulsos de undas rectangular de 1 milliampere de currente directe, e le tracias del campos derivational, establite al superficie del corpores, esseva registrate.

2. Es describite methodos pro calcular vectores derivational e triangulos de Burger ab le campos derivational. Le datos assi computate es presentate in forma tabular.

3. Le campo del derivation III es un representation approximative del ideal configuration derivational. Le campo del derivation II e specialmente le campo del derivation I devia significativemente ab le configuration ideal.

4. Le analyse theoric del distorsiones derivational que resulta del massa intracardiac de sanguine monstra que componentes tangential de dipolos a currente intra le myocardio contribue relativemente pauco al deflexiones in electrocardiogrammas del extremitates. In despecto de distorsiones derivational resultante del sanguine intracavitari, le fortias electromotor del corde es probabilemente registrate in un maniera quasi-vectorial.

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SELECTIVE PHONOCARDIOGRAPHY

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THE purpose of clinical phonocardiography is twofold: (a) a registration of the cardiac sounds and murmurs which may be correlated with data revealed by auscultation (in this regard, it is an auxiliary, bedside method); and (b) a correct recording of those same sounds and murmurs which permits their study and their interpretation (in this regard, it is an independent graphic method.)†

The "hybrid" types of phonocardiographs of the period between 1920 and 1938 (the apparatus of Boulitte in France, Siemens in Germany, and Cambridge in this country) gave tracings which were unsatisfactory for either of the two above purposes. The Sanborn phonocardiographs, developed since 1939 in this country, tried to fulfill the two main purposes of phonocardiography by means of the "logarithmic" and "stethoscopic" methods.[1,2] The tracings were first recorded by two different crystal microphones (stethocardiette), then by a single electromagnetic microphone provided with two different types of filters (twin-beam). The stethoscopic method excludes only those low-pitched vibrations (below 10 per second) which have no acoustic meaning, and faithfully reproduces the others; it is, therefore, useful for scientific analysis of the sound tracing. The "logarithmic tracing" emphasizes the high-pitched vibrations similarly to the human ear and is useful for correlation and control of clinical auscultation.

Unfortunately, two types of diastolic murmurs are frequently of difficult reproduction: the low-pitched apical murmur of mitral stenosis and the higher-pitched basal murmur of aortic insufficiency. If the vibrations are pure and there are no extrinsic noises created in the chest or the room, amplification may reveal them better. However, usually other vibrations are amplified too and the tracing does not become more distinctive through amplification.

Emphasis of the high-pitched vibrations can be obtained by mechanical filters (diaphragms of various thickness applied to the chest piece of the microphone). However, these diaphragms severely decrease the amplitude of *all*

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†This definition is more comprehensive than that adopted by a European Committee of Standardization of Phonocardiography which limits the method to the first purpose.[9]

vibrations so that increased amplification may compensate for this and bring out the higher-pitched vibrations only if their magnitude is fairly high: faint murmurs are not recorded.

We considered it necessary to undertake a new study dealing with the practical problem of obtaining better records of the most common murmurs whenever they are of poor amplitude.

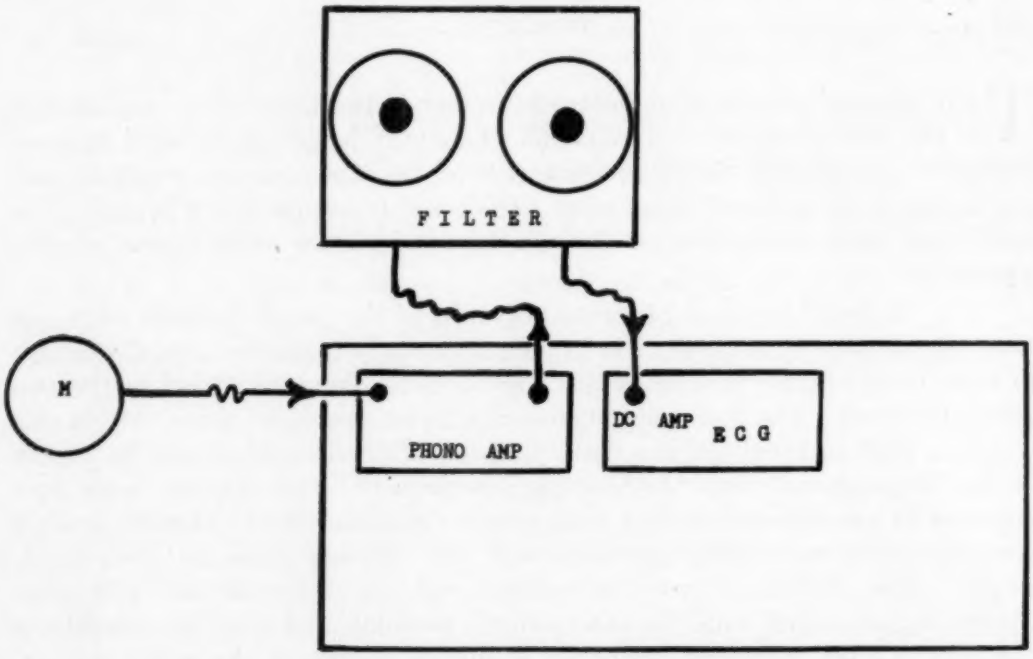

Fig. 1.—Connections of filter with the amplifiers of phonocardiograph.

TECHNIQUE

A variable band-pass filter* is connected with a Sanborn twin-beam† by means of two cables terminating with two jacks. The microphone placed over the chest of the patient is plugged as usual in the "phone" amplifier. The *input cable* of the filter picks up the electric impulses generated by the microphone from one of the "audiophone" outlets. The *output cable* of the filter is plugged into the DC input of the ECG amplifier (Fig. 1). Thus, the sound vibrations are transformed into electrical impulses, amplified, filtered, amplified again, and recorded by the ECG channel. As a result, two superimposed and simultaneous tracings are recorded, a "stethoscopic" phonocardiogram (phono channel) and a "filtered" phonocardiogram (ECG channel). Filtration is obtained by manipulating the two knobs of the variable filter (Fig. 1). The latter is acti-

*Model 310-AB, supplied by the Krohn-Hite Instrument Company, Cambridge, Mass.

†We wish to thank Dr. A. Miller of the Sanborn Company for a preliminary study which permitted the connection of the two devices.

vated by the 125 volts current. The frequency dials are calibrated logarithmically from 19 to 200,000 vibrations per second for both the high and the low cut-off frequencies. The filter allows the elimination of any frequency from 19 upwards and 200,000 downwards. The band-pass response (Fig. 2) shows a sharp line above and below the desired band of frequencies.

By trial and error, it was found that the best way to operate the device is the following: (a) the microphone is placed over the desired area and the auscultatory phenomena are checked through electric auscultation (audiophone); (b) the variable filter is activated by plugging its cable into a wall socket; its input and output cables are then connected with the phonocardiograph (see above); (c) the low and high pass filters are set at the desired limits; (d) by manipulating the "sensitivity" knob of the ECG amplifier, the amplitude of vibrations of the filtered phonocardiogram is regulated.

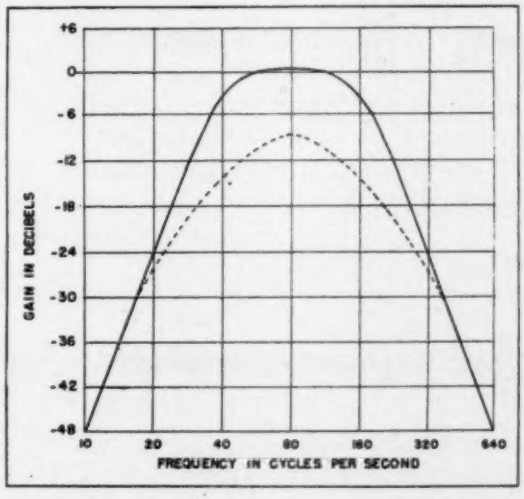

Fig. 2.—Solid curve shows the band-pass response of the Model 310-AB. Dotted curve is the response of a similar filter with independent RC sections.

RESULTS

Our study was made in eight normal adults and in thirty abnormal cases. As several of the patients had multiple valvular lesions, the following breakdown shows a higher figure. The following murmurs were studied:

Apical systolic murmurs	15
Apical or midprecordial diastolic (or presystolic) murmurs	16
Aortic systolic murmurs	11
Aortic diastolic murmurs	10
Pulmonic systolic murmurs	5
Total	57

Apical systolic murmurs: In thirteen out of fifteen cases, the best band for demonstrating the murmurs was 100 to 150. Two cases had murmurs of lower frequencies (Figs. 3,*A* and 4,*B*).

Apical diastolic murmurs: In fifteen out of sixteen cases, the best band for demonstrating the murmurs was 60 to 100 (at times 60 to 80 was even better) (Figs. 3,*A* and 4,*B*).

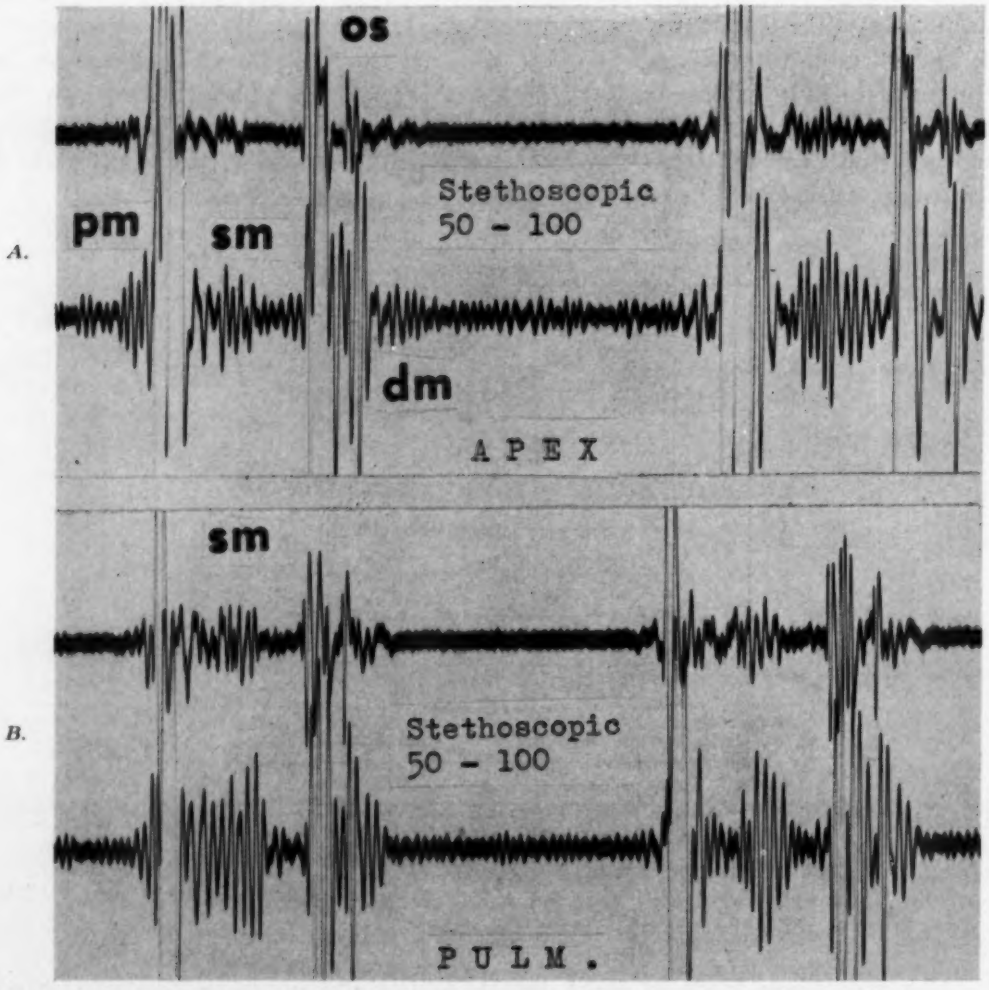

Fig. 3.—A 39-year-old woman with rheumatic heart disease, mitral valve disease, and severe dilatation of the pulmonary artery. *A, Apical tracings:* Above, Stethoscopic tracing (faint systolic murmur and opening snap of the mitral valve). Below, Band 50 to 100 (presystolic murmur, systolic murmur, opening snap, and diastolic rumble); *os* = opening snap; *pm* = presystolic murmur; *sm* = systolic murmur; *dm* = middiastolic murmur. *B, Pulmonic tracings:* Above, Stethoscopic tracing (systolic murmur and opening snap). Below, Band 50 to 100 (large systolic murmur, opening snap with after vibrations).

Aortic systolic murmurs: In nine out of eleven cases, the best band was between 100 and 150; one case had better tracings at a lower level (70 to 100) and one at a higher level (170 to 200) (Figs. 5,*D*, 6,*C*, 7,*A*, and 7,*C*).

Aortic diastolic murmurs: In eight out of ten cases, the best band was between 150 and 200; one case had the best tracing at a lower level (100 to 150), and one at a higher level (250 to 300) (Figs. 5,*D* and 6,*C*).

Pulmonic systolic murmurs: In all six cases, the best band was between 150 and 200 (Figs. 3,*B* and 7,*B*).

As a result of the above study, it was concluded: (1) that tracings at the apex or midprecordium should be recorded with a band between 60 and 110; this would demonstrate both the systolic and the diastolic murmurs of mitral defects; (2) that tracings over the aortic or pulmonic areas or at Erb's point for murmurs caused by aortic or pulmonic stenosis or insufficiency should be recorded with a band between 150 and 200. This would demonstrate both the systolic and the diastolic murmurs. Occasional patients with lower-pitched basal murmurs or higher-pitched (musical) apical or basal murmurs may have the best tracing in slightly different bands, but the above two bands (60-110 apex; 150-200 base) have been found adequate even for those cases.

Comparison of our tracings with those obtained by means of the conventional methods (stethoscopic for the low-pitched murmurs; logarithmic with or without mechanical filters for the high-pitched) revealed such a superiority for the new method of "selective phonocardiography" (Figs. 4, 5, and 6) that this deserves to be used for routine phonocardiography. This superiority is particularly apparent for murmurs of poor magnitude (faint murmurs), of high pitch (soft murmurs), or low pitch (rumbles).

DISCUSSION

The frequency characteristics of the cardiac murmurs were studied by Cabot and Dodge[3] in 1925 and by Williams and Dodge[4] in 1926. Listening through electric filters, they recognized that, while low-pitched murmurs had vibrations in the range 120 to 400, nine out of eleven cases had vibrations below 120. The moderately high, or high-pitched, murmurs nearly always had vibrations between 240 and 400 cycles per second with some reaching up to 660; they also had important components below 120 cycles. Some high-pitched components up to 1,000 were occasionally found. The energy of the murmurs was not found uniformly distributed because, in each individual case, a large percentage of the total energy was in a relatively narrow band. As these studies were made by means of auscultation, they were not devoid of possible sources of error. Moreover, the filters used in 1925 were likely to be less accurate than those recently developed.

With a similar method of filtering and listening to cardiac murmurs, Butterworth and associates[5] found most systolic murmurs between 80 and 120; the mitral diastolic murmurs between 40 and 100; and the diastolic murmurs of aortic and pulmonic insufficiency between 100 and 200.

"Calibrated" phonocardiography has been considered as a theoretically sound method for nearly twenty years. Introduced by Mannheimer[6] in 1938, the term meant that the tracings were recorded by a microphone which gave a standard type of response for a certain magnitude of vibration, and by means

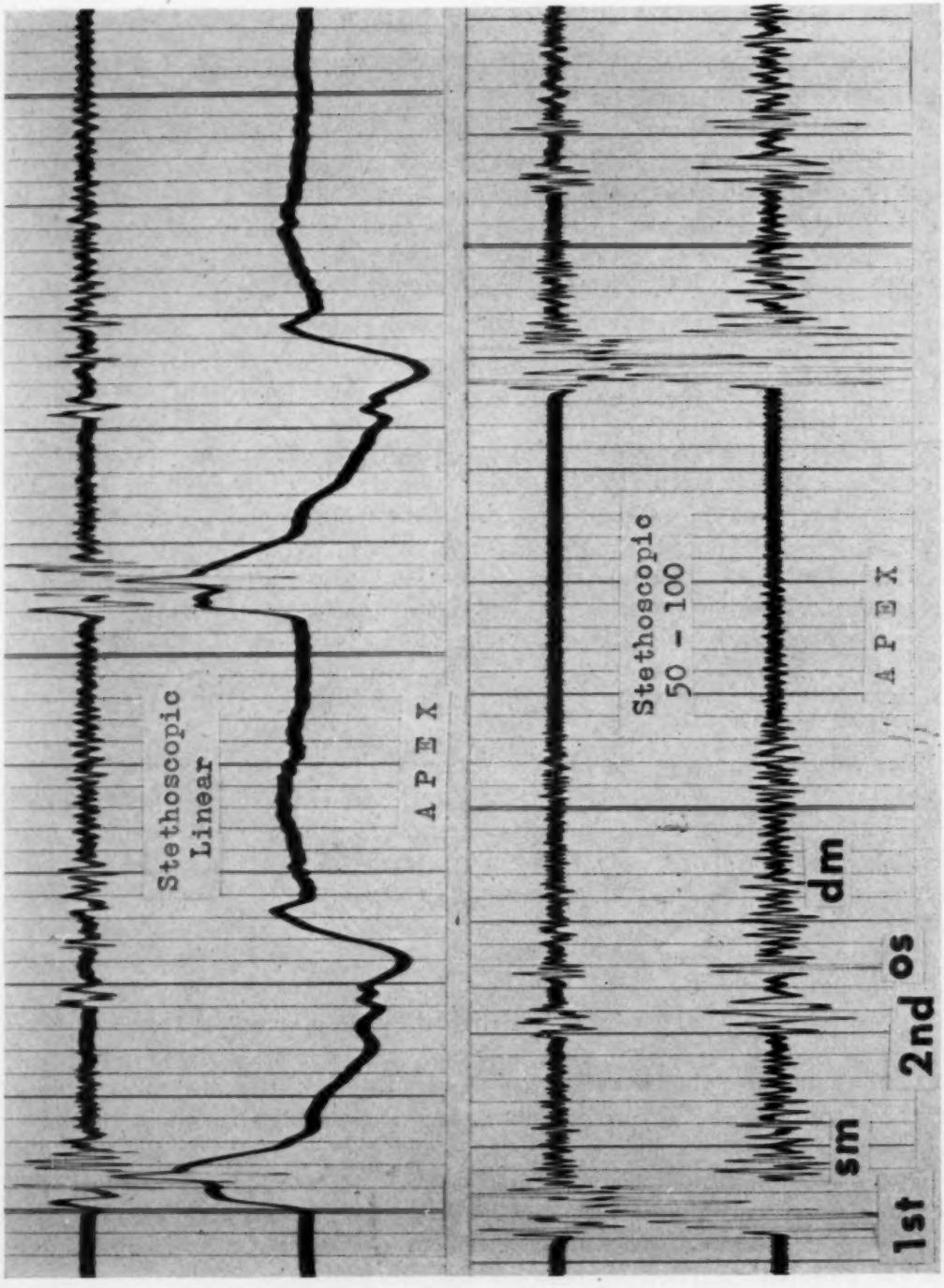

Fig. 4.—Young woman with mitral stenosis and insufficiency. *Apical tracings.* *A*, Stethoscopic and linear tracings (faint systolic murmur, small opening snap, faint diastolic rumble). *B*, Above, Stethoscopic tracing. Below, Band 50 to 100 (large systolic murmur, large opening snap, large vibrations of the diastolic rumble). *os* = opening snap; *dm* = middiastolic murmur.

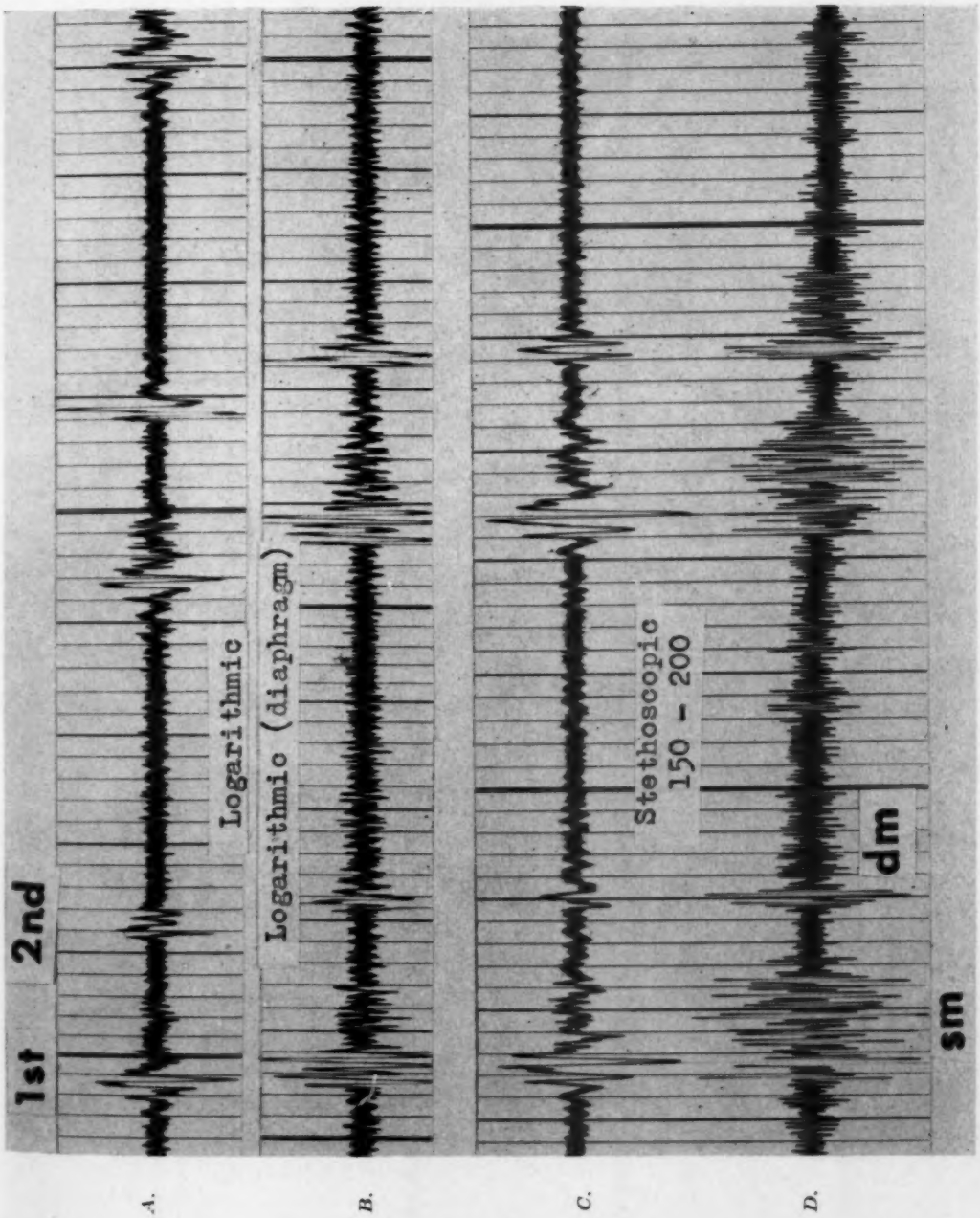

Fig. 5.—A 79-year-old woman with atherosclerosis of the aorta; loud systolic and faint diastolic murmur over aortic area. *Aortic tracings.* *A*, Logarithmic tracing (faint systolic and diastolic murmurs). *B*, Logarithmic tracing with diaphragm (larger vibrations). *C*, Stethoscopic tracing (faint systolic). *D*, Band 150 to 200 (large, diamond-shaped systolic murmur; large diastolic murmur in decrescendo). *sm* = Systolic murmur; *dm* = diastolic murmur.

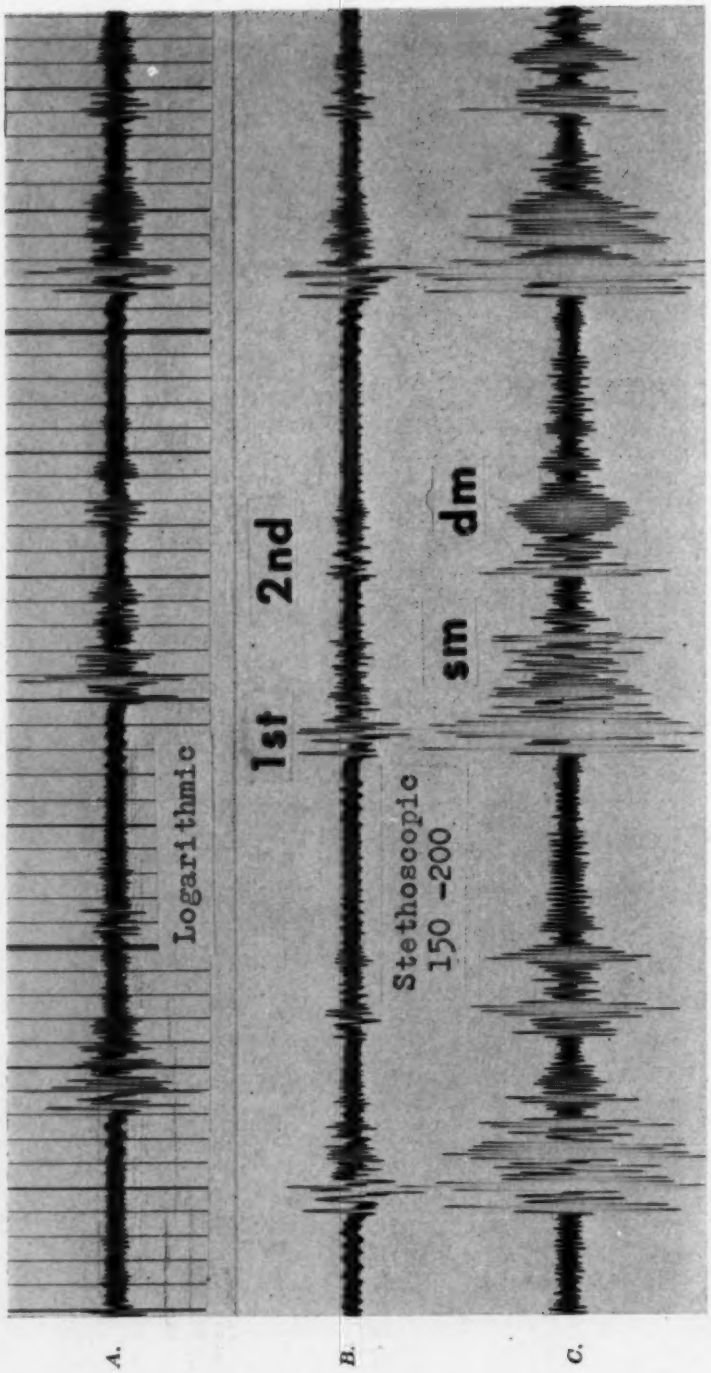

Fig. 6.—A 70-year-old woman with fibrosis and calcification of the aortic valve. Loud systolic, faint diastolic aortic murmur. *Aortic tracings. A*, Logarithmic tracing (faint systolic, minimal diastolic murmur). *B*, Stethoscopic tracing (less well-recorded diastolic murmur). *C*, Band 150 to 200 (large systolic and diastolic murmurs). Time lines removed for better vision. *sm* = Systolic murmur; *dm* = diastolic murmur.

of "filters" which excluded certain frequencies. The final tracing was recorded by means of a six-channel galvanometer recording the ECG and five separate phonocardiograms. Apart from the complexity of the apparatus and the difficulty of reading so many simultaneous tracings, two main criticisms can be advanced to this method:

a. The various filters are not juxtaposed, eliminating adjoining bands of frequencies; some are partly juxtaposed, others are one within the other.

b. As no additional amplification is used, filtration increases the visibility of certain vibrations only by "default"; murmurs of poor magnitude may entirely disappear.

A new method of "filtered" phonocardiography was described by Maass and Weber[7] in 1952. The apparatus is similar to that of Mannheimer and should have the same objections. However, there is a marked progress in the system of filtration. Five low-pass filters cut off certain frequencies from below upwards: below 35, below 70, below 140, and below 250. There still is no sufficient selectivity for the various bands and no adequate amplification for the "faint" vibrations.

Our analysis of murmurs roughly coincides with the findings of Butterworth. Most vibrations of clinical importance are in the low and medium frequency bands. Even in cases having "high-pitched" vibrations up to 600 per second or higher, there may be such a predominance of energy in the vibrations below 200 that the best tracing is still that recorded between 150 and 200.

In our study, frequencies above 400 per second were recorded only with marked amplification. Those above 600 were of minimal importance and difficult to register because extreme amplification increases the registration of extraneous vibrations (some of them are unavoidable because they originate within the chest).

As proved by the listing of data, two bands of frequencies were found to be clinically significant, that between 60 and 110 and that between 150 and 200. Even in those rare cases where an adjoining band would give the optimum tracing, the two bands still give useful tracings, far superior to those currently recorded.

We investigated the possibility that filtering the vibrations according to the above-described method would lead to emphasis of unimportant diastolic vibrations which might be misleading for diagnosis. Observations made in normal subjects (Figs. 8,*B* and 9) and patients with an enlarged heart having no diastolic murmurs revealed that it is not so. The third and fourth sounds are usually of low frequency (between 20 and 60) (Fig. 8,*A*). A large and complex fourth (atrial) sound may cause some high-pitched vibrations which, through filtering, might simulate a presystolic murmur. These are easily recognized by comparison of the "selective" tracing with a "stethoscopic" tracing. The same applies to higher-pitched vibrations which may follow the second sound or accompany the third.

Among the first results of this study we should include: (a) the recording of an apical systolic murmur in most cases of mitral stenosis (moderate regurgi-

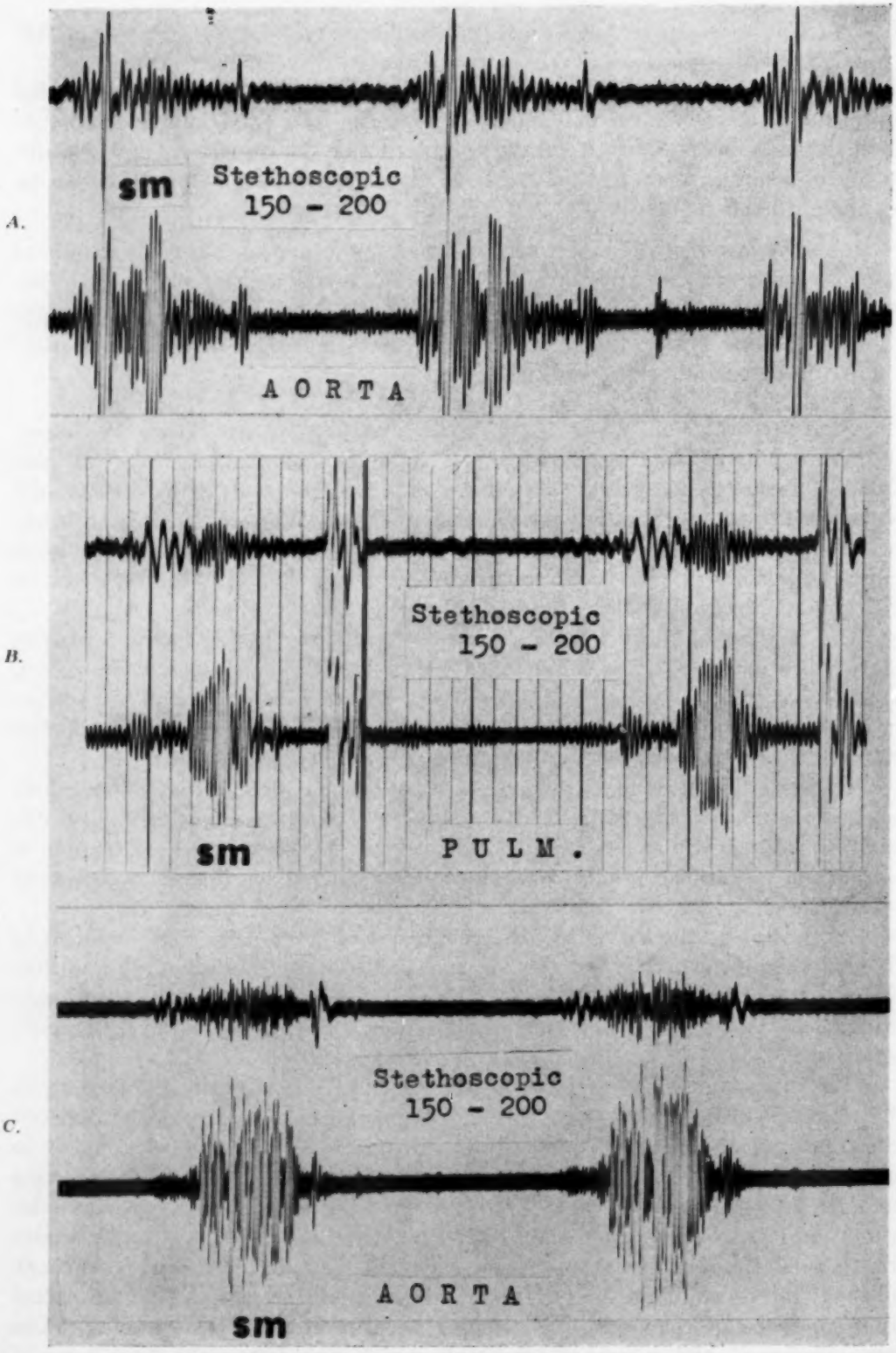

Fig. 7.—Basal murmurs. *A*, Case of aortic stenosis. *Aortic tracings.* Above, Stethoscopic tracing. Below, Band 150 to 200 (better record of systolic murmur). *sm* = Systolic murmur. *B*, Adolescent with musical systolic murmur. *Pulmonic tracings.* Above, Stethoscopic tracing. Below, Band 150 to 200 (best recording of diamond-shaped murmur). *sm* = Systolic murmur. *C*, A 79-year-old man with moderate calcific aortic stenosis. Above, Stethoscopic tracing. Below, Band 150 to 200 (best recording of systolic, diamond-shaped murmur). *sm* = Systolic murmur.

tation had been recognized by means of other methods); (b) the recording of apical diastolic rumbles of mitral stenosis which were poorly recorded by conventional methods; (c) the recording of "soft," early-diastolic murmurs of aortic insufficiency, which otherwise defied recording.

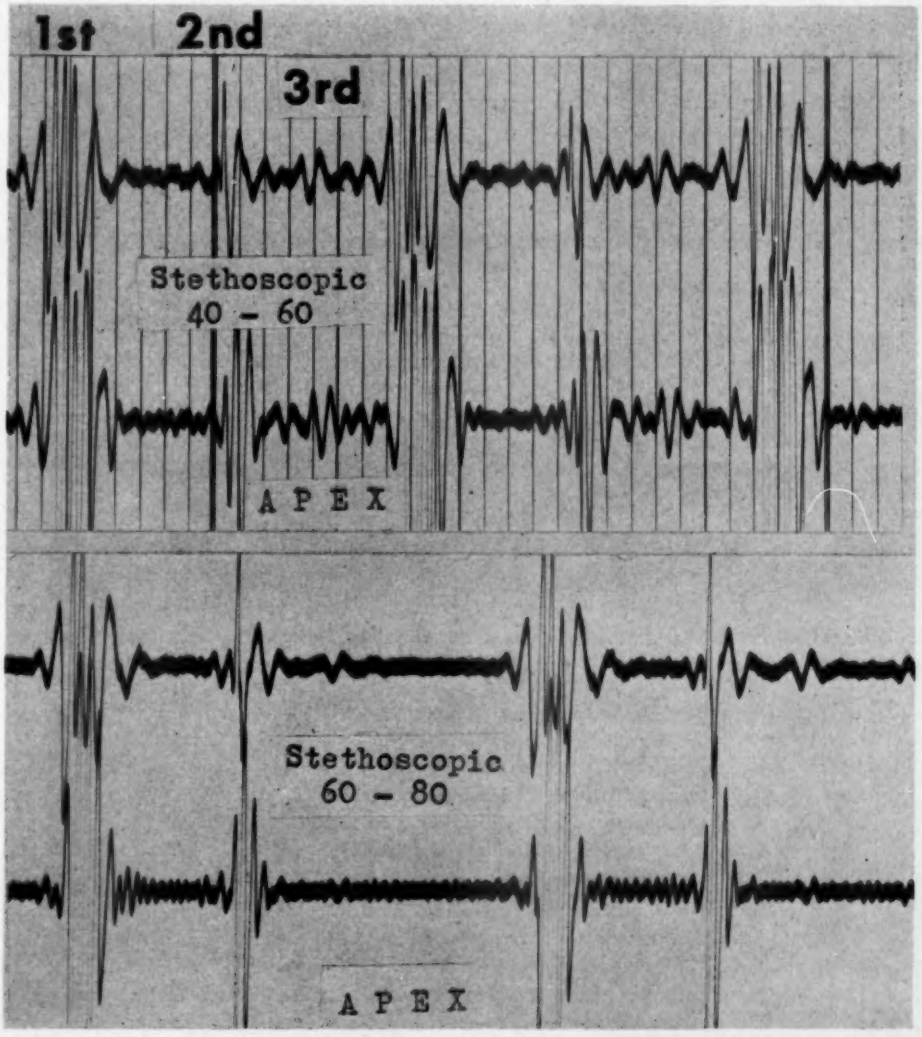

Fig. 8.—Fifteen-year-old girl with faint systolic murmur. *Apical tracings.* *A*, Above, Stethoscopic tracing. Below, Band 40 to 60 (large third sound). *B*, Above, Stethoscopic tracing. Below, Band 60 to 80 (faint systolic murmur).

PRACTICAL SUGGESTIONS

The above studies should be followed by certain technical suggestions:

1. To maintain the present type of recording an electrocardiogram and a "stethoscopic" tracing over all areas in order to obtain a comprehensive picture of the various frequencies.

2. To record apical, midprecordial, and tricuspid tracings also in the low band (60 to 110) for recognition of mitral or tricuspid murmurs.

3. To record tracings at the aortic and pulmonic areas and at the midprecordium also in the high band (150 to 200) for recognition of aortic or pulmonic murmurs.

4. To record a "linear" tracing (low frequency tracing) together with a "stethoscopic" tracing whenever this is useful for interpretation of extra sounds.

5. To abandon "logarithmic" tracings.

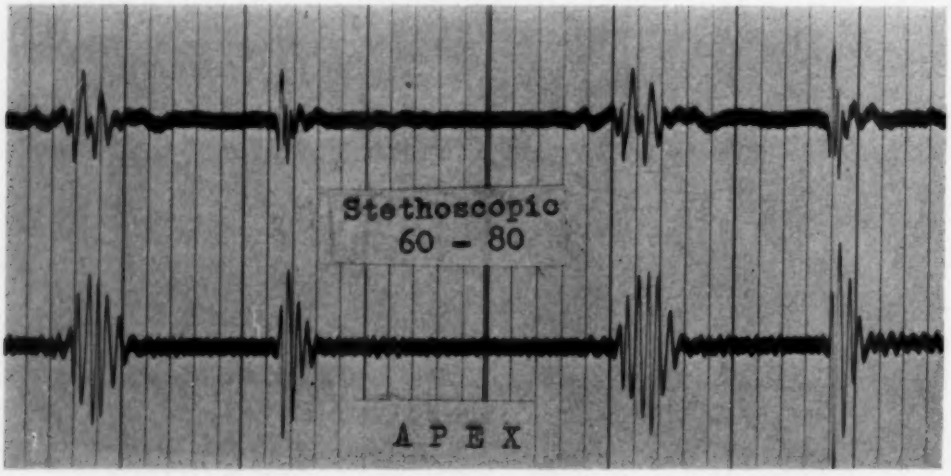

Fig. 9.—Normal man of 32 years. *Apical tracings.* Above, Stethoscopic tracing. Below, Band 60 to 80.

The routine method should be as follows:

1. Apex—Stethoscopic and ECG.
2. Midprecordium—Stethoscopic and ECG.
3. Pulmonic area—Stethoscopic and ECG.
4. Aortic area—Stethoscopic and ECG.
5. Tricuspid area—Stethoscopic and ECG.
6. Apex—Stethoscopic and low band (60–110).
7. Midprecordium—Stethoscopic and low band (60–110).
8. Midprecordium—Stethoscopic and high band (150–200).
9. Pulmonic area—Stethoscopic and high band (150–200).
10. Aortic area—Stethoscopic and high band (150–200).
11. Tricuspid area—Stethoscopic and low band (150–200).
12. Apex—Stethoscopic and linear.
13. Midprecordium—Stethoscopic and linear.
14. Epigastrium—Stethoscopic and linear.

This routine method of investigation, based on the recording of 14 tracings, should be compared to that of 13 tracings previously recommended by one of the authors (A.A.L.).[8]

Adequate filters might be incorporated in the phonocardiographs, so that the two required bands would be obtained by simply switching an indicator knob to different positions.

SUMMARY

1. Problems dealing with the registration of either apical or basal diastolic murmurs of poor magnitude are discussed. Current methods of phonocardiography are reviewed.

2. Eight normal subjects and thirty abnormal cases were studied by means of a variable band-pass filter with additional amplification. The various frequencies of the cardiac murmurs were analyzed. A band between 60 and 110 vibrations per second was found adequate for magnifying and recording murmurs caused by mitral defects. A band between 150 and 200 was found adequate for magnifying and recording murmurs caused by aortic insufficiency.

3. A routine method of study of cardiac murmurs, called "selective phonocardiography" is outlined. It is based on the use of the two above bands, in addition to "stethoscopic" phonocardiograms.

SUMMARIO IN INTERLINGUA

1. Es discutite problemas in le registration de murmures diastolic, o apical o basal, de debile magnitude. Le methodos currente de phonocardiographia es passate in revista.

2. Octo subjectos normal e 30 casos anormal esseva studiate per medio de un variabile filtro a banda con amplification additional. Le varie frequentias del murmures cardiac esseva analysate. Un banda de inter 60 e 110 vibrationes per secunda se monstrava adequate pro magnificar e registrar murmures causate per defectos mitral. Un banda de inter 150 e 200 vibrationes per secunda se monstrava adequate pro magnificar e registrar murmures causate per insufficientia aortic.

3. Es delineate un methodo de studiar murmures cardiac, appellate "phonocardiographia selective." Le methodo es basate super le uso del duo supramentionate bandas in combination con phonocardiogrammas "stethoscopic."

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THE MITRAL OPENING SNAP IN THE QUANTITATIVE DIAGNOSIS OF MITRAL STENOSIS

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INTRODUCTION

THE diagnostic aim in patients with mitral stenosis has been modified since surgical treatment of this valvular disease has been made possible. In addition to the more qualitative diagnosis, quantitative values concerning the indication for operative treatment and the evaluation of the operative result have proved necessary.

This can be best achieved by cardiac catheterization leading to intracardiac pressure recordings and the determination of cardiac output according to Fick's principle. Information concerning the varying degrees of mitral stenosis can also, however, be achieved by phonocardiography, as long as the intensity of the heart sound, its character, and its duration are ignored, and only the interval between the second heart sound and the mitral opening snap is considered. These findings have been proved by comparative examinations with intracardiac pressure recordings and phonocardiograms (PCG) in 100 cases of mitral stenosis. Details will be given in the following report.

HISTORICAL REVIEW

The interpretation of "doubling" of the second heart sound has remained obscure for a long time. Guttmann[3] in 1872, who was the first to consider the sound phenomena as an expression of the mitral valve opening, was followed by Sansom[8] a few years later (1881). Rouchès[7] in 1888 coined the expression "clac d'ouverture de la mitrale," this term being accepted in the following years by the Anglo-American and, later, by the German literature. Schölmerich[9] (1951) pointed out the dependence of the interval between the second heart sound and mitral opening snap upon factors which promote or hinder the blood flow into the left auricle. According to him, the varying durations of the interval are related to changes in the pressure of the left auricle. Similarly the variations of the interval in cardiac arrhythmias, accompanied by different durations of diastole, can be explained (Margolies and Wolferth,[4] 1932; Messer and associates,[5] 1951; Stein, Schölmerich, and Engelbertz,[10] 1952; Mounsey,[6]

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1953; Grosse-Brockhoff,[2] 1954). Pressure changes in the left auricle were also considered responsible for the appearance of a mitral opening snap following operative treatment when none had been present before (Bayer, Boden, and Derra,[1] 1953).

METHODS

One hundred patients with pure or functionally predominant mitral stenosis were examined. The mean "pulmonary capillary" pressure ("PC"), as a measure of the pressure in the left auricle, and the interval between the beginning of the second heart sound and the first vibrations of the mitral opening snap were compared. The following conditions must be considered for these comparative examinations:

1. The simultaneous recording of the "PC" pressure and the phonocardiogram (about 200 H_7).

2. The clarity of the "PC" pressure curve in the sense of a "transmitted copy" of the left auricular pressure curve.

3. The level of brachial artery pressure.

Expl. 1. Experiments have shown that a correlation between the mean "PC" pressure and the interval can be obtained only by simultaneous recording. Phonocardiograms registered at different moments and under changing circumstances show different intervals. Apparently the reasons for this are changes in the left auricular pressure with varying heart rates and cardiac outputs.

Expl. 2. Pressure curves, recorded after wedging of the catheter into a terminal branch of the pulmonary artery, which could not be analyzed clearly as "PC" pressure curves, were nct used for determining the mean pressure in the left auricle.*

Expl. 3. The relation of the mitral opening snap to the second heart sound represents the interval between the aortic valve closure and the mitral valve opening. It depends upon:

a. The pressure difference in the left ventricle between the moment of aortic valve closure and the moment of mitral valve opening.

b. The slope of pressure decrease between aortic valve closure and mitral valve opening, i.e., during the isometric relaxation of the left ventricle.

Because, toward the end of the isometric relaxation, the ventricular pressure declines more gradually, changes in the auricular pressure have, therefore, a relatively marked influence on the interval between the second heart sound and mitral opening snap. Changes in aortic pressure do not have this significance.

The relationship is illustrated in Fig. 1, which shows a left ventricular pressure curve with a superimposed aortic pressure curve.

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*The fact that a relation between the second heart sound-mitral opening snap interval and the mean "PC" pressure can be traced only if the curve shows the required clarity, supports indirectly its interpretation as a "transmitted copy" of the pressure curve of the left auricle (Wolter, Bayer, Loogen, and Rippert).[11]

It can be seen from Fig. 1 that the aortic pressure must be taken into consideration if a relation between the pressure of the left auricle and the interval between the second heart sound and the mitral opening snap is to be shown. The systolic pressure in the brachial artery can be used for this, because this pressure has the most constant relation to the pressure at the time of aortic valve closure. This pressure is closely related to the pressure at the moment of aortic valve closure and shows the smallest variability with aortic valvular defects.

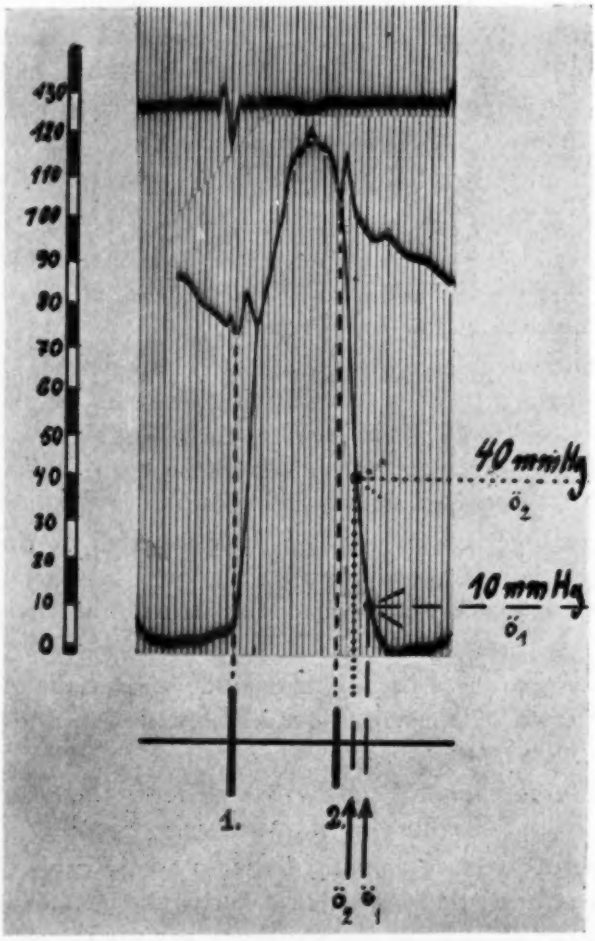
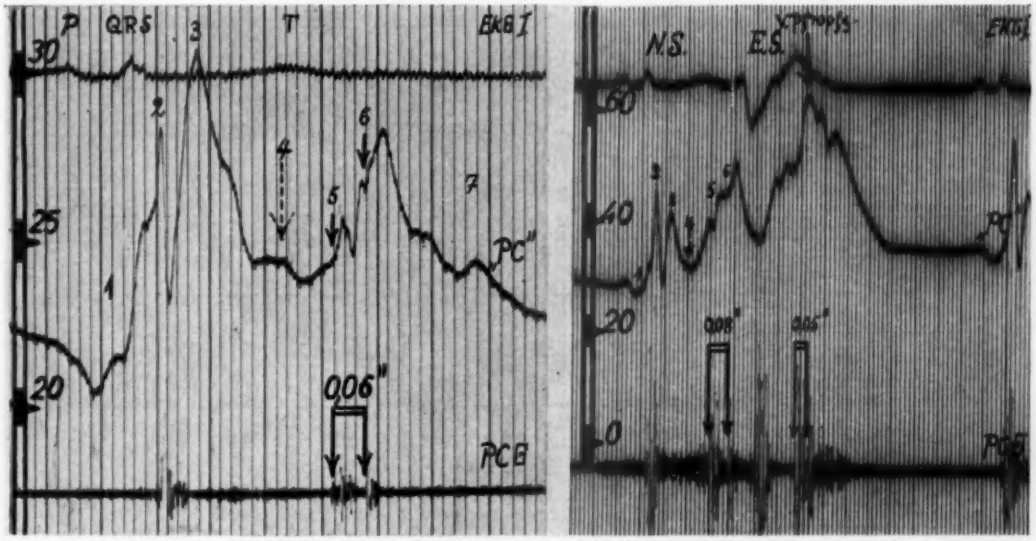


Fig. 1.—Pressure tracings of left ventricle and aorta (superimposed) in a patient with ventricular septal defect. The figure demonstrates the dependence of the interval between second heart sound and mitral opening snap on the height of the left auricular pressure. $\ddot{o}_1$ = Assumed auricular pressure of 10 mm. Hg; $\ddot{o}_2$ = Assumed auricular pressure of 40 mm. Hg; 1. = first heart sound; 2. = second heart sound.

The slight inaccuracy regarding the absolute pressure height may be ignored as only an empiric comparison is needed. The necessity of considering the systemic arterial pressure in the determination of the mean left auricular pressure by phonocardiography also follows from the observations shown in Fig. 2. If the brachial artery pressure is elevated by the application of Arterenol (nor-

adrenalin), the duration of the interval is changed in a manner unexplained by the change in the auricular pressure. Previous to administration of Arterenol the systolic blood pressure amounted to 115 mm. Hg and the mean pulmonary capillary pressure to 25 mm. Hg, with an interval of 0.06 second. Following injection of 0.5 mg. Arterenol the systolic arterial pressure was elevated to 165 mm. Hg, with a mean pulmonary capillary pressure of 40 mm. Hg and an interval of 0.08 second. This change of the interval would signify a pressure fall in the left auricle unless the increase of systemic blood pressure, with the associated lengthening of the interval, is taken into account. This interpretation is also supported by the change of the interval following premature beats in the form of a bigeminus (with fixed coupling) which occurred during the examination



A. *B.*

Fig. 2.—Shows the ECG (Lead I), the "PC" pressure curve and the phonocardiogram of a patient affected with combined mitral stenosis and insufficiency before (*A*), and after (*B*) injection of 0.5 mg. Arterenol (noradrenalin).

***A*, The interval of 0.06 second corresponds to a mean left auricular pressure of approximately 25 mm. Hg. The "PC" pressure curve demonstrates: (1) the wave of left auricular contraction; (2 and 3) time of A-V closure and of opening of the aortic valve; (4) the negative wave at the time of ventricular contraction, diminished by mitral regurgitation; (5 and 6) time of closure of the aortic valve and the opening of the mitral valve, respectively; (7) the pressure fall during ventricular relaxation.**

***B*, After injection of Arterenol mean "PC" pressure increased, and also a bigeminal rhythm appeared. One sees in the "PC" pressure curve at the time of P of the sinus rhythm an enlarged wave of auricular contraction due to closed A-V valve. In the PCG there is an alternation of the interval between second heart sound and mitral opening snap (see text). N.S. = Normal beat; E.S. = premature beat; V. pfropfg. = enlarged wave of auricular contraction against closed A-V valve.**

(Fig. 2). Whereas the interval during normal sinus rhythm, as mentioned above, was 0.08 second, there was a narrowing to 0.05 to 0.06 second for the premature beats. Such interval alternations could not be explained by the changes of left auricular pressure as these were too insignificant. Also, without registration of the aortic or brachial artery pressure during the arrhythmia, it

can be assumed that the markedly varying diastolic periods of the normal rhythm and of the premature beats gave rise to a considerable change in the systolic pressure of the left ventricle. The alternation of the ventricular pressure may consequently serve as a sufficient explanation for the observed alternation in the phonocardiogram.

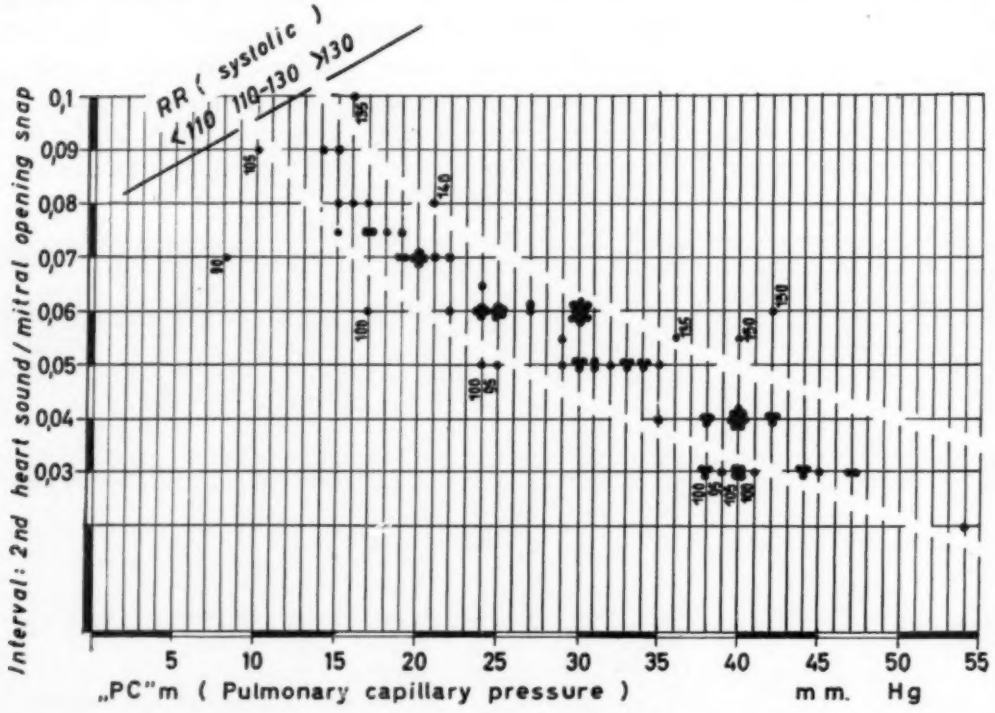


Fig. 3.—Shows the dependence of the interval between second heart sound and mitral opening snap upon the mean "PC" pressure and the systemic arterial systolic pressure (after RIVA-ROCCI) in 100 patients.

RESULTS

1. *Relationship of Pressure Height in the Left Auricle to the Interval Between Second Heart Sound and Mitral Opening Snap.*—The diagram given in Fig. 3 is constructed in consideration of the previously mentioned conditions for a comparison between the mean pressure of the left auricle and the interval between second heart sound and mitral opening snap. The results of 100 patients with different degrees of mitral stenosis were evaluated. Because the arterial blood pressure can influence the interval, the patients were divided into 3 groups with regard to the systemic systolic blood pressure. The lowest pressure was 90 mm. Hg, the highest 150 mm. Hg. In the majority of cases (80) the pressure was between 110 and 130 mm. Hg. "PC" pressure values of all cases included in the 3 groups are plotted against the corresponding sound intervals. It is seen that the mean slope of the curve increases in the range of low "PC" pressure, i.e., decreases or increases of pressure in the zone of lower pressure lead to major changes or the interval. This relationship follows from the decreasing slope of the ventricular pressure curve toward the end of the isometric relaxation. The

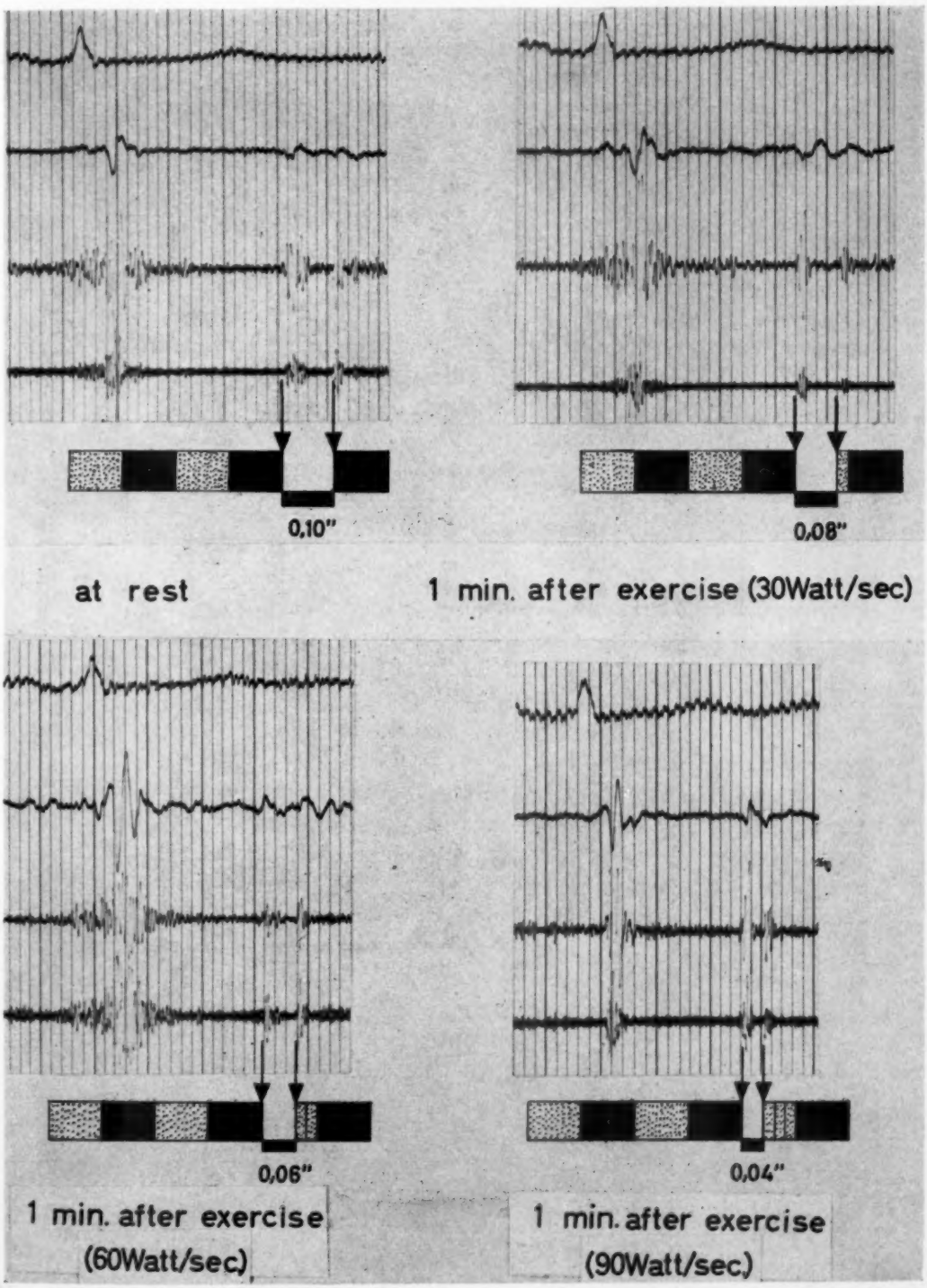


Fig. 4.—Increasing shortening of the interval between second heart sound and mitral opening snap in the PCG one minute after varying grades of exercise (Watts per second). The insignificant shortenings after 30 and 60 Watts per second exercise over 5 minutes exclude severe grades of mitral stenosis.

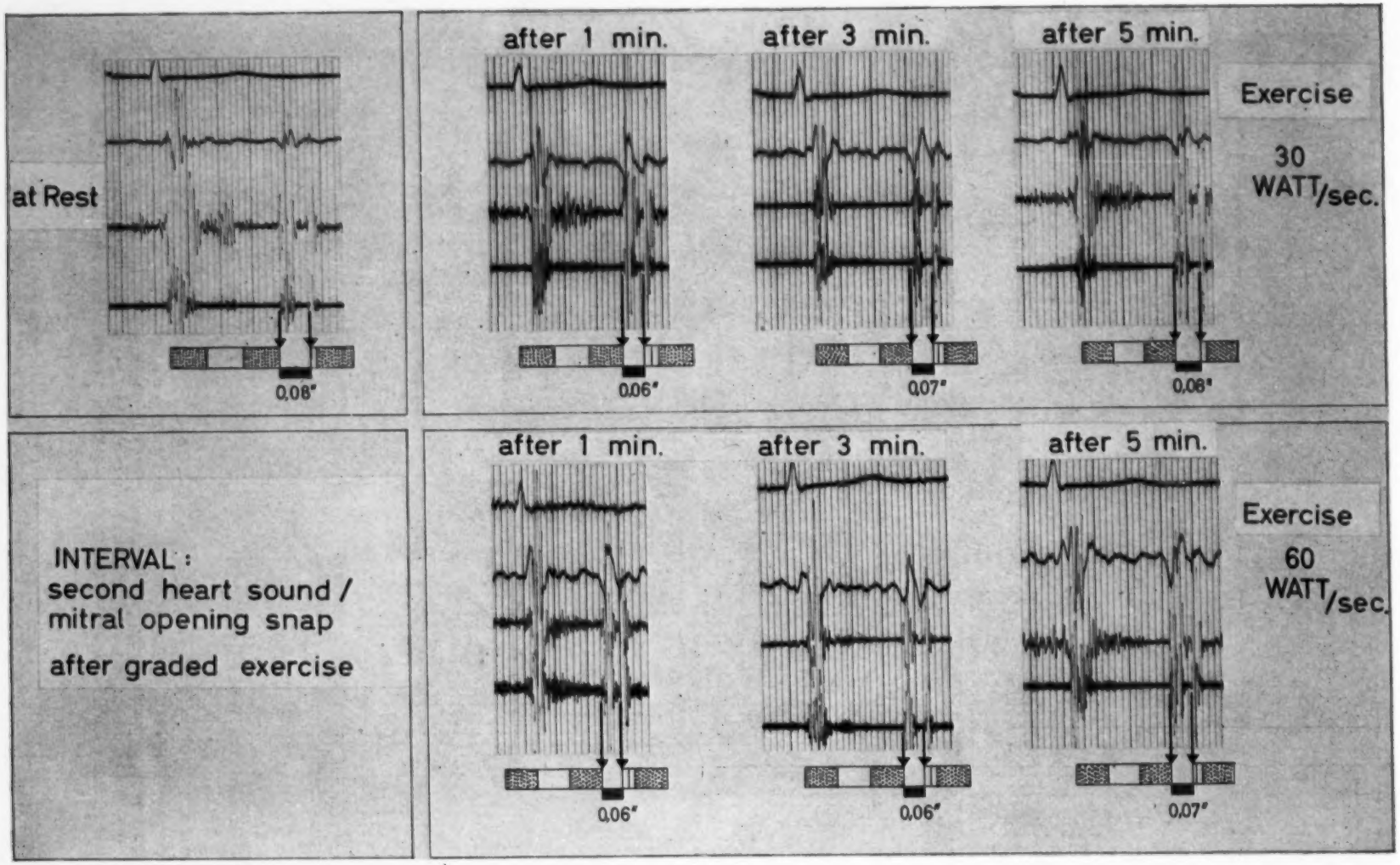


Fig. 5.—Shortening of the interval between second heart sound and mitral opening snap after exercise of 30 and 60 Watts per second, with varying duration of return to the basic values in the same patient.

relatively small deviations are explained by the variation of the systemic systolic pressure between 110 and 130 mm. Hg and, possibly, by a small individually changing slope of the declining part of the ventricular pressure curve. The other cases do not correspond to the observations of the 80 patients in regard to their systolic blood pressure and show larger deviations. They lie in the direction of a shortening when remaining below 110 mm. Hg and in the direction of a prolongation of the interval between second heart sound and mitral opening snap when exceeding 130 mm. Hg. Consequently, an approximate determination of the mean left auricular pressure from the phonocardiogram is possible, if, apart from the measured interval, the systemic systolic blood pressure is also considered. As the mean pressure of the left auricle is increased in close relation to the degree of the mitral stenosis, this purely clinical procedure permits—to a certain degree—a quantitative diagnosis of mitral stenosis. It must, however, be stressed that the sole consideration of the mean auricular pressure was not proved sufficient for the determination of the area of the mitral valve opening, as changes of pulse frequency and cardiac output remain inconsidered in this procedure.

To avoid this difficulty, patients of varying heart rate and cardiac output were examined under conditions of basal metabolism. In this manner comparison is possible. If, under these circumstances, a narrow interval up to 0.05 second is found, a high-grade mitral stenosis with an opening area of less than 1 $cm.^2$ can be assumed, as long as there is no tachycardia with an insufficient diastolic inflow time. On the other hand, larger intervals do not allow the conclusion of a slight mitral stenosis at all heart rates. In such cases the changes of the PCG at gradually increased rates of exercise are of important diagnostic value. Likewise, intervals which even at moderate exercise (30 Watt/sec. for 5 minutes) suggest a considerable increase in auricular pressure at moderately increased heart rate indicate a stenosis of severe degree. If an exercise of 30 or 60 Watt per second is followed by only a slight shortening of the interval (e.g., from 0.08 to 0.06 second) such a result usually excludes the most extreme degrees of stenosis (Fig. 4). Besides the absolute shortening of the interval with a given exercise for a period of 5 minutes, one must also bear in mind the speed of return to the basic value when evaluating the degree of stenosis (Fig. 5). Two extreme types of reactions can be distinguished. There are, however, many transitional stages between them. To illustrate this point, the same shortening of interval in two patients with corresponding initial intervals must be appraised differently when the time of return to the initial interval is of a significant difference (Fig. 6,*A* and *B*). In the first case there is an initial interval of 0.08 second and a shortening to 0.06 second following exercise of 30 Watt per second. The return to the basic value had not been reached 8 minutes later (*A*), whereas in the other case the corresponding return occurred in 5 minutes (*B*). From this it may be assumed that the circulatory stress in the first case is considerably greater than in the second one. In such cases it cannot be clearly judged how far these various responses are the expression of a different valvular stenosis or of varying regulation of the blood vessels.

This procedure permits a quantitative evaluation of a patient's exercise tolerance. Formerly, this was possible only by cardiac catheterization with gradually increased exercise. The special advantage of this method lies in its relative simplicity and its brevity. For the patient it means a harmless examination which can be repeated many times.

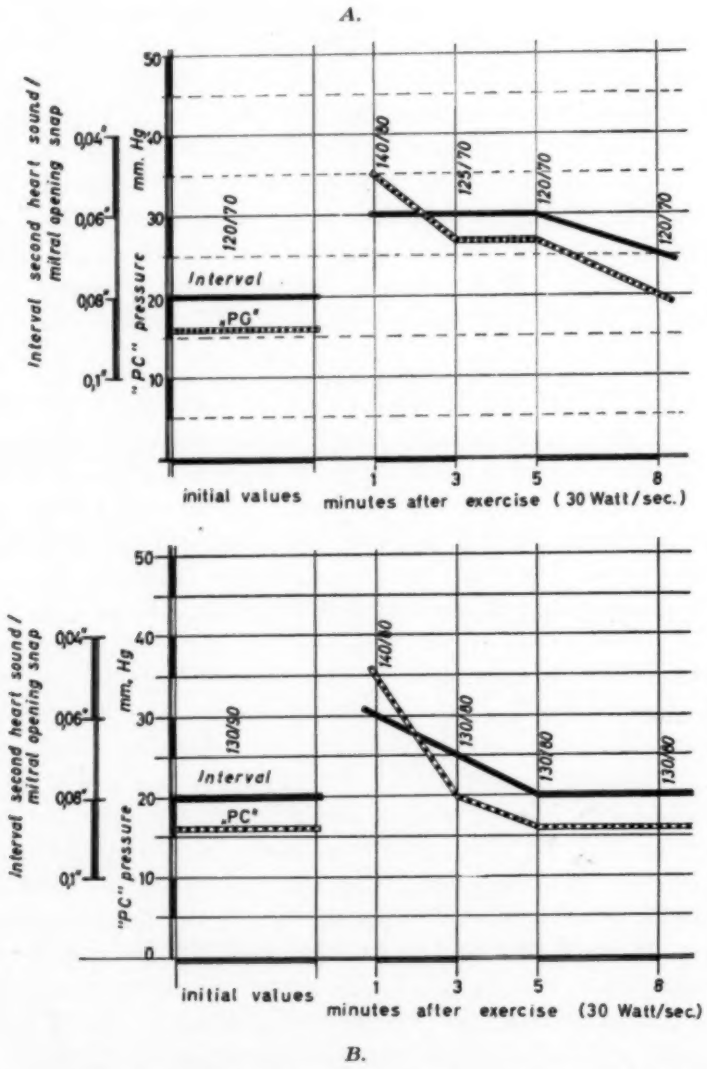


Fig. 6.—Varying returns of the interval between second heart sound and mitral opening snap to the basic value after exercise with 30 Watt/sec. over a period of 5 minutes in two patients (*A* and *B*). Furthermore, the figure shows the changes of the left auricular pressure ("PC" pressure) related to the systemic systolic blood pressure (after RIVA-ROCCI).

2. *Changes in the Second Heart Sound—Mitral Opening Snap Interval After Mitral Valvotomy.*—Besides the use of this procedure with regard to indications for surgical treatment, its performance postoperatively has proved especially successful, as it allows control examinations at any time after con

valescence. The improvement of exercise tolerance, obtained by operative treatment, can thus be easily shown and quantitatively judged to a satisfactory degree. If the operative results are good, one finds a prolongation of the interval at rest compared with the initial value before the operation (Fig. 7). Simultaneously, an increase of exercise tolerance with only a small shortening of the interval in proportion to the degree of exercise can be observed, or a quicker return to the initial values.

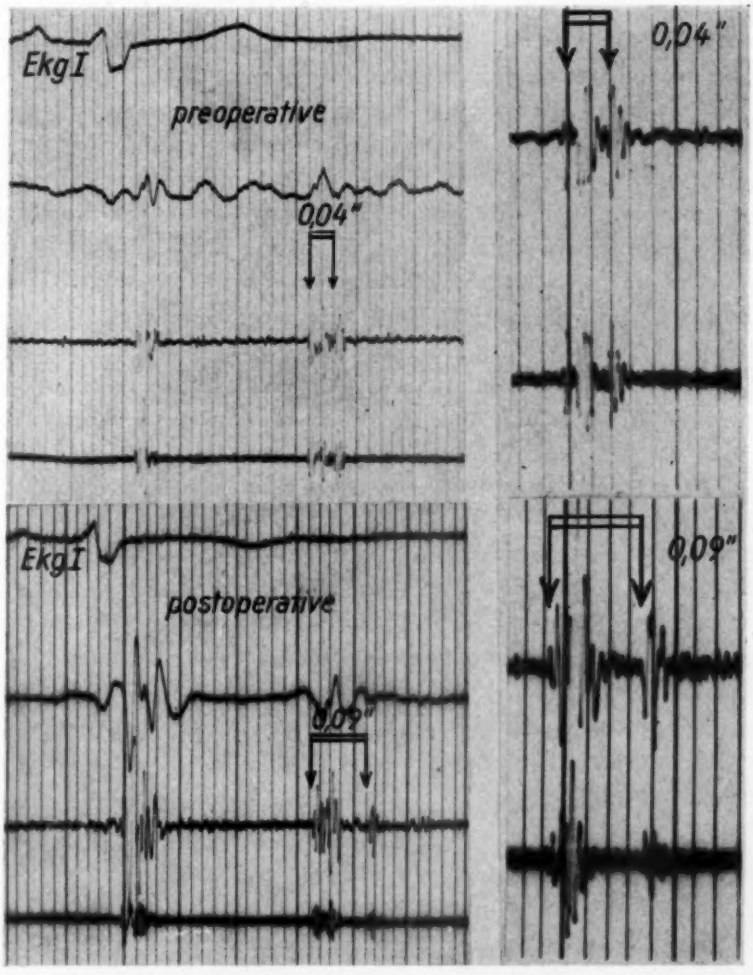


Fig. 7.—ECG and PCG in a patient with mitral stenosis before and after operative treatment. The heart rate was the same in both recordings. One sees an increased interval between second heart sound and mitral opening snap after surgical treatment as compared to preoperative findings. Right: Enlarged representation of the waves at the end of the systolic phase.

SUMMARY

1. On the assumption that the interval between the second heart sound and the mitral opening snap depends largely on the height of the left auricular pressure, comparative examinations between these two factors have been made

in 100 patients with clinical mitral stenosis. As a measure of left auricular pressure the mean "pulmonary capillary" pressure was used.

2. The following conditions were observed: (a) simultaneous recordings of PCG and "PC" pressure curve; (b) formal clarity of the "PC" pressure curve in the sense of recording a "transmitted copy" of the left auricular pressure curve; (c) in addition, the systolic blood pressure in the brachial artery was taken and correlated with the other data.

3. A relationship between the interval (second heart sound mitral opening snap) and the height of the mean pressure in the left auricle was demonstrated. Thus, the interval shortened as mean "pulmonary capillary" pressure (and so, presumably, mean left auricular pressure) increased.

4. Blood pressure affected the second heart sound-mitral opening snap interval in the sense of tending to shorten it below 110 mm. Hg systolic pressure and prolonging it above 130 mm. Hg systolic pressure. However, variations from the most common range between 110 and 130 mm. Hg were not frequent enough to allow an exact definition of these parameters.

5. Consequently, the phonocardiogram allows conclusions about the pressure increase in the left auricle which in turn is closely related to the degree of mitral stenosis.

6. The pressure increase in the left auricle for different degrees of exercise could be inferred from changes in the interval and consequently conclusions about the exercise tolerance of the patients could be drawn. The absolute shortening after exercise, as well as the time of return to the starting interval, must be considered.

7. In many cases this harmless and time-saving procedure has made unnecessary the performance of cardiac catheterization before deciding on surgical treatment. Further, it allows unlimited control examinations for later evaluation of the increase of exercise tolerance after mitral valvotomy.

8. After successful mitral valvotomy two changes were observed. First, there occurred a prolongation of the interval compared to preoperative values. Second, the interval shortened much less with exercise or returned more quickly to its pre-exercise value.

SUMMARIO IN INTERLINGUA

In 100 patientes con clinic stenosis mitral, examinationes comparative esseva executate inter le altor del pression median "pulmono-capillari" e le intervallo inter le secunde sono cardiac e le aperiente clic mitral. Il esseva possibile demonstrar un relation inter iste duo factores. Assi le intervallo se diminueva quando le pression se augmentava.

Il es necessari prender in consideration le systemic pression sanguinee, proque il esseva constatate que illo affice le intervallo, tendente a diminuer lo quando le pression systolic esseva infra 110 mm. Hg e a augmentar lo quando le pression systolic esseva supra 130 mm. Hg.

Consequentemente le phonocardiogramma permitte conclusiones in re le augmento de pression in le auriculo sinistre e le grado de stenosis mitral.

Ab alterationes del intervallo con varie grados de exercitio il esseva possibile derivar conclusiones in re le toleration a exercitio. In isto il es necessari prender in consideration le diminution absolute e le tempore del retorno al intervallo initial.

Le methodo etiam permitte illimitate examines de controlo pro le subsequente evalutation del augmento de toleration a exercitio post commissurotomia mitral.

We wish to extend our gratitude to Dr. Andrew P. Adams for his help in preparing the English translation.

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THE ELECTROCARDIOGRAM ONE YEAR AFTER ACUTE MYOCARDIAL INFARCTION

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THE serial electrocardiographic changes of acute myocardial infarction are well known. There is no precise information available, however, as to the length of time that electrocardiographic abnormalities persist after acute myocardial infarction, though such information would be of definite value.

Vander Veer and Edwards[1] studied 102 electrocardiograms with absent initial positive deflection in Lead V of Wolferth and Wood (R.A. electrode on the cardiac apex and L.L. electrode on the left leg) and Lead IV_R (L.A. electrode on the apex and R.A. electrode on the right arm) and forty-six electrocardiograms with a small initial positive deflection (2.0 mm. or less) in the same leads. They stated that when the initial positive deflection in these precordial leads is absent, it probably rarely returns to normal. They also stated that the QRS abnormalities in the precordial lead seemed less susceptible to change (return to normal) than did the T wave alterations in this lead. Wallace[2] studied 108 cases showing a significant Q_3. He stated that the Q wave is often the only remaining graphic evidence in the electrocardiogram of the residue of a pathologic process which at one time was acute. Contratto, Robinson, and Levine[3] studied serial tracings in seventeen patients with acute anterior wall infarction varying from six weeks to two years. At the time of this study the polarity of precordial Lead IV was opposite to the present convention. They stated that in fourteen cases with an absent Q wave (i.e., with an absent R wave in the convention of today) in only one case did the Q wave return to normal (i.e., initial R return). In eleven of their seventeen cases the T wave of the precordial lead became upright (i.e., inverted in convention of today). In eight of these it remained upright (i.e., in the new convention, inverted). Bohning and Katz[4] studied 650 records from 200 patients with recent myocardial infarctions. They stated that in serial electrocardiograms the record often stops short of complete recovery and may persist for a long period of time at a later stage of evolution. No definite statement was made in regard to time span. Katz[5] stated that following myocardial infarction, if the coronary insufficiency has been compensated, the electrocardiogram tends to return to normal. In addition, the QRS

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deformities which appear at the onset of the attack are often the only abnormalities which persist. These QRS configurations may remain unchanged for years. Master and associates[6] reporting on 202 cases of coronary occlusion stated that the electrocardiogram returned completely to normal in twenty-eight cases and almost to normal in fifteen others. They said that the electrocardiogram returned practically to normal in more than one-fifth of the cases, indicating that the absence of typical electrocardiographic changes does not exclude previous coronary occlusion. These electrocardiograms returned to normal in a variable interval ranging from less than one month to four years. The majority returned to normal within one year. These authors studied Leads I, II, III, and IV.

The present study was undertaken to determine the evolution of changes in the electrocardiogram one year following acute myocardial infarction and to compare this "one year" electrocardiogram with the tracing which had been taken at about the time of the patient's discharge from the hospital following the acute attack. In practically all cases the earlier electrocardiogram followed the acute attack by six weeks to two months and seemed to have stabilized.

MATERIAL

The electrocardiograms of fifty-one patients with acute myocardial infarction were chosen for study. In each patient the serial electrocardiograms following the acute attack showed typical changes of myocardial infarction (i.e., significant Q waves were present in the appropriate leads). There were twenty-eight patients with the electrocardiographic changes of posterior wall myocardial infarction and twenty-four patients with those of anterior wall myocardial infarction. The electrocardiograms of one patient were those of a posterior wall infarct in the limb leads and an anterior wall infarct in the precordial leads (pattern of Roesler and Dressler[7]). There were thirty-nine male patients and twelve female patients. The "one year" electrocardiograms were obtained in most instances exactly twelve months after the first tracings, and in no instance less than nine months or more than fifteen months. No patients were studied in whom, during the year following the initial myocardial infarction there was suspicion of an additional infarction.

In the tracings of posterior wall infarction Leads II, III, aV_F and a right precordial lead were examined. In the tracings of anterior wall infarction Leads I, aV_L, and V_1 to V_6 were studied. Throughout the study of the precordial leads, we have been impressed as have other investigators with the lack of significance of an initial R wave which is 1 mm. or less in height (embryonal R) when it is followed by an S wave of considerable amplitude. In such a situation the S wave becomes a Q equivalent and for the purpose of comparison the S wave has been so considered. In this series the S wave or Q equivalent had an amplitude that was eight or more times the amplitude of the embryonal R wave. No electrocardiogram was considered to have an embryonal R wave when such a wave was a part of a normal progression of the R wave with increasing amplitude across the left precordium.

TABLE I

	LEAD II				LEAD III				LEAD aV_F			
	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.
"first"	0.03	1.0	4.0	−1.0	0.04	6.0	1.0	−3.0				
"1 yr."	0.04	2.0	2.5	0	0.04	6.5	1.5	−1.0				
"first"	0.02	2.0	10.0	−2.0	0.04	5.0	5.0	−3.0				
"1 yr."	0.02	1.0	9.0	1.0	0.04	4.0	4.0	−2.0				
"first"	0.02	1.5	5.0	−1.5	0.04	2.0	2.0	−2.0	0.02	1.0	2.0	−2.0
"1 yr."	0.03	1.5	8.0	1.0	0.04	2.0	4.0	2.0	0.04	1.5	6.0	2.0
"first"	0.04	3.0	0.5	−2.0	0.04	9.0	0	−4.0				
"1 yr."	0.04	3.0	2.0	0	0.08	11.0	1.0	1.0				
"first"	0.02	2.0	4.0	−2.5	0.04	9.0	3.1	−6.0	0.04	3.5	2.0	−4.0
"1 yr."	0.02	1.0	4.0	2.0	0.04	12.0	1.0	−3.0	0.04	4.0	2.0	−1.5
"first"	0.02	1.0	3.0	−3.0	0.06	5.0	7.0	−7.0				
"1 yr."	0.00	0	7.0	−0.5	0.06	7.0	3.0	−5.0				
"first"	0.04	1.0	1.0	1.0	0.08	6.5	0	±1.0	0.06	4.0	1.0	±1.0
"1 yr."	0.04	2.0	3.5	0	0.05	5.0	1.0	1.0	0.06	2.0	2.0	1.0
"first"	0.00	0	0.5	1.0	0.00	0	1.0	−1.0	0.04	1.0	1.0	0.5
"1 yr."	0.02	1.0	1.0	1.0	0.00	0	1.0	±0.5	0.08	3.0	0.5	1.0
"first"	0.04	2.5	3.0	1.5	0.06	10.0	2.0	−1.0	0.05	5.0	1.0	−1.0
"1 yr."	0.06	5.0	1.0	−1.0	0.08	17.0	0	−3.0	0.06	11.0	1.0	−2.0
"first"	0.04	2.0	3.0	−3.0	0.04	4.0	1.5	−4.0	0.04	3.0	2.0	−4.0
"1 yr."	0.04	2.0	1.5	−1.0	0.04	9.0	1.0	−4.0	0.04	4.0	1.0	−2.0
"first"	0.03	2.0	10.0	−1.5	0.04	5.0	7.0	−3.0				
"1 yr."	0.04	2.0	13.0	0	0.04	5.0	5.0	0				
"first"	0.04	3.0	5.0	−3.0	0.06	6.5	1.0	−6.0				
"1 yr."	0.04	2.0	10.0	1.0	0.04	4.0	5.0	−2.0				
"first"	0.03	3.0	1.0	−3.0	0.08	6.0	1.0	−7.0	0.08	3.0	0	−5.0
"1 yr."	0.04	3.0	8.5	−1.0	0.06	8.0	7.0	−6.0	0.04	5.0	6.0	−4.0
"first"	0.02	1.0	6.0	0.5	0.08	4.0	0	−0.5	0.04	1.5	0.5	−0.5
"1 yr."	0.04	1.5	3.0	2.0	0.08	4.0	0	1.0	0.06	2.0	0	1.0
"first"	0.03	0.5	2.0	−0.5	0.04	6.0	1.0	−2.0	0.03	2.0	1.0	−1.0
"1 yr."	0.04	1.0	3.0	1.0	0.06	6.0	1.0	−1.0	0.04	1.5	2.0	−1.0
"first"	0.05	3.0	1.0	−3.0	0.08	10.0	0	−6.0	0.08	4.0	0	−4.0
"1 yr."	0.05	2.0	6.0	1.0	0.05	10.0	2.0	−1.0	0.05	3.0	1.0	−0.5
"first"	0.00	0	1.0	−3.0	0.07	8.0	0	−6.0	0.07	3.0	0	−4.0
"1 yr."	0.00	0	4.0	−0.5	0.08	5.0	0	−2.0	0.04	2.0	2.0	−1.0
"first"	0.03	3.0	4.0	−0.5	0.08	7.0	0	−3.0				
"1 yr."	0.03	2.0	5.0	0.5	0.08	6.0	0	−1.0				
"first"	0.02	1.5	10.0	−0.5	0.05	3.5	9.0	−3.0				
"1 yr."	0.02	1.0	10.0	0.5	0.05	4.0	8.0	−1.0				
"first"	0.06	2.0	2.5	−5.0	0.06	9.0	1.5	−5.0				
"1 yr."	0.06	4.0	2.0	−1.0	0.06	12.0	1.0	−2.0				
"first"	0.04	2.0	3.0	−2.0	0.04	6.0	2.0	−6.0	0.04	4.0	1.0	−4.0
"1 yr."	0.04	2.0	1.0	−1.0	0.05	5.0	1.5	−4.5	0.04	3.0	0.5	−2.5
"first"	0.04	1.5	2.0	−1.5	0.08	5.0	0	−2.0	0.08	2.5	0	−1.0
"1 yr."	0.03	2.0	3.0	−1.0	0.08	2.5	0	−1.0	0.04	2.0	2.0	−1.0
"first"	0.04	2.0	2.0	0.5	0.07	5.0	0	−5.0	0.04	2.0	0	−1.0
"1 yr."	0.02	1.5	3.0	2.0	0.05	3.0	0	−1.0	0.04	1.5	0	1.0
"first"	0.04	3.5	2.5	−1.0	0.07	5.0	0	−3.0				
"1 yr."	0.04	2.0	4.0	1.0	0.07	3.0	0.5	1.0				
"first"	0.02	1.0	1.0	−3.0	0.08	14.0	0	−4.5				
"1 yr."	0.00	0	2.5	−1.0	0.08	14.0	0.5	−2.0				
"first"	0.08	4.0	2.0	−2.0	0.08	19.0	2.0	−4.0				
"1 yr."	0.06	4.0	2.0	−2.0	0.08	13.0	2.0	−3.0				
"first"	0.02	1.0	7.0	−1.0	0.04	3.0	8.0	−2.0				
"1 yr."	0.03	1.5	10.0	1.0	0.06	5.0	11.0	−1.0				
"first"	0.04	7.0	4.5	−2.5	0.04	8.0	4.5	0.5	0.04	6.0	4.0	−1.0
"1 yr."	0.04	4.0	11.0	−1.0	0.04	3.0	4.0	±0.5	0.04	3.0	9.0	±1.0

QRS complex, RS-T segment, T wave, and Q-T interval were analyzed. The amplitude and duration of the Q waves were measured. The R wave amplitude was measured in all leads. The QRS duration was determined in Lead I in all anterior wall infarcts and Lead I and III in all posterior wall infarcts. Displacement of the RS-T segment was measured in all leads. The T wave was examined in all leads for direction of deflection and amplitude. The Q-T interval was measured in Lead I in anterior wall infarcts and Lead III in posterior wall infarcts. Lead II was not used because of the possibility of an isoelectric component of the QRS complex. The Q-T_C was determined by use of the Bazett Formula.[8]

Electrocardiograms taken at the time of the acute myocardial infarction will be referred to as "first" electrocardiograms or "first" tracings, and those taken about one year later as "one year" electrocardiograms or tracings.

I. POSTERIOR WALL INFARCTS

Measurements of the amplitude and duration of the Q wave, amplitude of the R wave, and the direction and amplitude of the T wave are recorded in Table I. The following information was obtained from these measurements.

A. *Lead II.*—

1. *Q wave:* In twenty-six of the "first" electrocardiograms Q waves were present in this lead. The Q wave amplitude varied from 0.5 to 7.0 mm. and the duration from 0.02 to 0.08 second. Q waves were present in twenty-five of of the "one year" electrocardiograms. The amplitude of Q increased in nine instances, decreased in eleven, and in seven it was unchanged. The duration of the Q wave had increased in nine instances, decreased in five, and in thirteen it was unchanged.

2. *R wave:* The amplitude of the R wave varied from 0.5 to 10.0 mm. in the twenty-eight "first" electrocardiograms. In the "one year" electrocardiograms the amplitude of the R wave varied from 1.0 to 13.0 mm. The amplitude of the R wave had increased in eighteen instances, decreased in seven, and in three it was unchanged.

3. *T wave:* In twenty-three of the twenty-eight "first" electrocardiograms the T wave was inverted, in five it was upright. Of the twenty-three instances with an inverted T wave in the "first" electrocardiogram, the T wave remained inverted in the "one year" electrocardiogram in ten, it had become upright in nine, and diphasic or isoelectric in four. In twenty-four of the twenty-eight "one year" electrocardiograms the T wave was less negative, in two it was more negative, and in two it was unchanged.

B. *Lead III.*—

1. *Q wave:* In twenty-seven of the "first" electrocardiograms Q waves were present in this lead. There was a QS pattern in ten of these. The amplitude of the Q wave varied from 2.0 to 19.0 mm. and the duration varied from 0.04 to 0.08 second. Q waves persisted in twenty-three of the "one year" electrocardiograms. There was a QS pattern in six of these. In four instances with

Q waves in the "first" tracing, initial R waves developed in later tracings. The amplitude of the Q wave varied from 2.0 to 17.0 mm., and the duration from 0.04 to 0.08 second. The amplitude of the Q wave had increased in nine instances, decreased in fourteen, and in four it was unchanged. The duration of the Q wave had increased in six instances, decreased in four and in thirteen it was unchanged.

2. *R wave:* The amplitude of the R wave varied from 1.0 to 9.0 mm. in the eighteen "first" electrocardiograms in which it was present. In the "one year" electrocardiograms the amplitude of the R wave varied from 1.0 to 11.0 mm. The R wave had increased in amplitude in five instances, decreased in ten, and in three it was unchanged.

3. *T wave:* The T wave was inverted in twenty-six of the twenty-eight "first" electrocardiograms. In one instance it was diphasic and in one instance upright. Of the twenty-six instances with an inverted T wave in the "first" electrocardiograms the T wave remained negative in twenty-one, became upright in three and in two was diphasic or isoelectric in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in twenty-six instances, in one it was more negative, and in one it was unchanged.

C. *Lead aV_F.*—

1. *Q wave:* Lead aV_F was available in fifteen instances in both the "first" and "one year" electrocardiograms. A Q wave was present in this lead in the "first" electrocardiogram in all fifteen instances. In five of these there was a QS pattern. The amplitude of the Q wave varied from 1.0 to 6.0 mm. and the duration from 0.02 to 0.08 sec. In fourteen of the "one year" electrocardiograms Q waves persisted; two of these had a QS pattern. In one instance with a Q wave in the "first" tracing, an initial 0.5 mm. R wave was present in the later tracing. The amplitude of the Q wave varied from 1.5 to 11.0 mm. and the duration varied from 0.02 to 0.06 sec. The amplitude of the Q wave had increased in six instances and decreased in nine. The duration of the Q wave had increased in four instances, decreased in four, and in six it was unchanged.

2. *R wave:* In ten of the fifteen "first" electrocardiograms with Lead aV_F, R waves were present. The amplitude of the R wave varied from 0.5 to 4.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 0.5 to 9.0 mm. The amplitude of the R wave had increased in four instances, decreased in four, and in two it was unchanged.

3. *T wave:* In thirteen of the fifteen "first" electrocardiograms the T wave was inverted, in one upright, and in one diphasic. Of the thirteen instances with an inverted T wave in the "first" electrocardiograms, the T wave remained negative in nine and became upright in five in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in twelve instances, more negative in one, and in two it was unchanged.

D. *Right Precordial Lead.*—A right precordial lead, C_1, was available in fourteen instances in both the "first" and "one year" electrocardiograms. There was an initial R wave in all fourteen instances in the "first" electrocardiograms. The R wave persisted in the "one year" electrocardiograms in all instances.

The T wave was upright in twelve of the fourteen instances in the "first" electrocardiograms, in two instances it was diphasic (one of these individuals had sustained a pulmonary infarct; the second individual had a congenital lesion, interventricular septal defect, in addition to the myocardial infarction). In the "one year" electrocardiograms the T wave was upright in twelve of the fourteen instances. The T wave had increased in positivity in two instances, decreased in two, and in ten it was unchanged.

RS-T SEGMENT

The electrocardiograms of patients receiving digitalis were not included in the following analysis of RS-T deviations.

A. *Lead II.*—There were no significant deviations of the RS-T segments in this lead.

B. *Lead III.*—In twenty-three of the twenty-eight "first" electrocardiograms the RS-T segment was isoelectric, in five instances it was elevated. In the "one year" electrocardiograms the RS-T segment became isoelectric in three of the instances in which it had been elevated in the "first" tracings. In one instance the RS-T segment elevation decreased and in one the elevation increased in the "one year" electrocardiogram.

C. *Lead* aV_F.—In thirteen of the fifteen "first" electrocardiograms the RS-T segment was isoelectric, in two it was elevated. In the "one year" electrocardiograms in one of these instances the RS-T segment was isoelectric and in the other the elevation was unchanged. In one instance in the "one year" electrocardiogram there was a 1.0 mm. elevation of the RS-T segment which had been isoelectric in the "first" tracings.

QRS DURATION

In the "first" electrocardiograms the greatest QRS duration was 0.14 sec. (right bundle branch block), shortest 0.06 sec., average 0.08 sec. In the "one year" electrocardiograms, the greatest QRS duration was 0.13 sec. (right bundle branch block), shortest 0.05 sec., average 0.08 sec. The QRS duration had increased in four instances, decreased in five, and in nineteen it was unchanged.

Q-T_c INTERVAL

In the "first" electrocardiogram the longest Q-T_c was 0.48 sec., shortest 0.36 sec., average 0.43 sec. In the "one year" electrocardiograms the longest Q-T_c was 0.48 sec., shortest 0.36 sec., average 0.42 sec. The Q-T_c was increased in nine instances, decreased in sixteen, and in three it was unchanged.

II. ANTERIOR WALL INFARCTION

Measurements of the amplitude and duration of the Q wave, the amplitude of the R wave, and the direction and amplitude of the T wave for Leads I and aV_L are recorded in Table II.

TABLE II

	LEAD I				LEAD aV_L			
	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.
"first"	0.00	0	4.0	1.5	0.00	0	4.0	1.0
"1 yr."	0.00	0	2.0	0.5	0.00	0	3.0	−0.5
"first"	0.08	2.0	0	−1.5	0.06	1.5	1.5	−2.5
"1 yr."	0.08	1.5	0	−1.0	0.06	1.5	1.0	−1.5
"first"	0.02	1.5	5.5	1.5	0.02	1.5	3.0	1.0
"1 yr."	0.04	1.5	7.0	1.0	0.02	1.0	5.0	0.5
"first"	0.00	0	6.0	−1.5	0.00	0	3.5	−2.0
"1 yr."	0.00	0	8.0	2.0	0.00	0	5.0	1.0
"first"	0.00	0	3.0	−2.0	0.00	0	2.0	−1.0
"1 yr."	0.00	0	4.0	−0.5	0.00	0	2.0	−0.5
"first"	0.00	0	8.0	−1.0	0.00	0	5.0	−1.0
"1 yr."	0.00	0	8.0	−1.0	0.00	0	2.0	−1.0
"first"	0.02	0.5	2.0	−1.5	0.02	0.5	4.0	−2.0
"1 yr."	0.02	1.0	3.0	−0.5	0.04	1.0	7.0	−1.0
"first"	0.02	0.5	2.0	−0.5	0.01	0.5	1.5	−0.5
"1 yr."	0.02	1.0	2.5	0.5	0.02	1.0	2.5	0
"first"	0.03	1.5	5.0	−2.0	0.04	4.0	8.0	−2.0
"1 yr."	0.03	1.0	4.0	−1.0	0.04	5.0	6.0	−1.5
"first"	0.03	1.5	1.0	−1.0	0.03	1.5	3.0	−1.5
"1 yr."	0.00	0	9.0	−0.5	0.04	1.0	9.0	−1.5
"first"	0.00	0	1.0	−4.0	0.00	0	1.0	−3.0
"1 yr."	0.00	0	4.0	−3.0	0.00	0	1.0	−4.0
"first"	0.04	2.0	3.0	−1.0	0.04	4.0	5.0	−2.0
"1 yr."	0.00	0	7.0	−2.0	0.04	5.0	10.0	−4.0
"first"	0.02	3.0	4.5	−5.0				
"1 yr."	0.04	1.5	5.0	−1.0				
"first"	0.00	0	6.0	−1.5	0.00	0	4.0	−1.0
"1 yr."	0.00	0	6.0	1.0	0.00	0	4.0	0.5
"first"	0.02	0.5	2.0	−2.0	0.04	1.0	3.0	−2.0
"1 yr."	0.03	1.0	5.0	−1.0	0.03	2.0	7.0	−2.0
"first"	0.02	2.0	8.0	−3.0	0.00	0	7.0	−2.0
"1 yr."	0.03	1.5	9.0	−1.5	0.00	0	3.0	−1.0
"first"	0.04	1.0	13.0	1.0	0.04	2.0	12.0	0.5
"1 yr."	0.02	2.0	17.0	1.5	0.03	2.0	16.0	1.0
"first"	0.00	0	9.0	−2.0				
"1 yr."	0.00	0	12.0	1.0				
"first "	0.00	0	3.0	−1.0				
"1 yr."	0.00	0	5.0	1.0				
"first"	0.00	0	0.5	−2.0				
"1 yr."	0.00	0	5.0	−1.0				
"first"	0.00	0	3.0	−1.5				
"1 yr."	0.00	0	8.0	0				
"first"	0.02	1.0	5.0	−4.0				
"1 yr."	0.00	0	9.0	−2.0				
"first"	0.02	1.0	4.0	−2.0				
"1 yr."	0.02	1.0	8.0	0				
"first"	0.07	3.0	3.0	−4.0				
"1 yr."	0.07	5.0	2.0	−1.0				

A. *Lead I.—*

1. *Q wave:* In fourteen of the twenty-four "first" electrocardiograms, Q waves were present. In one of these there was a QS pattern. The amplitude of the Q wave varied from 0.5 to 3.0 mm. and the duration varied from 0.02 to

0.08 sec. Q waves were present in eleven instances in the "one year" electrocardiograms; one of these had a QS pattern. The amplitude of the Q wave varied from 1.0 to 5.0 mm. and the duration varied from 0.02 sec. to 0.08 sec. The amplitude of the Q wave had decreased in seven instances, increased in five, and in two it was unchanged. The duration of the Q wave had increased in four instances, decreased in four, and in six it was unchanged.

2. *R wave:* An R wave was present in twenty-three "first" electrocardiograms. The amplitude of the R wave varied from 1.0 to 17.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 2.0 to 17.0 mm. The amplitude of the R wave had increased in eighteen instances, decreased in three, and in two it was unchanged.

3. *T wave:* The T wave was measured in twenty-four "first" electrocardiograms. It was inverted in twenty-one instances and upright in three. In the "one year" electrocardiograms T was inverted in fourteen instances, upright in eight, and isoelectric in two. Of the twenty-one instances of inverted T wave in the "first" electrocardiograms the T remained negative in sixteen instances and became upright in five in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in twenty instances, more negative in three, and in one it was unchanged.

B. *Lead aV_L.*—

1. *Q wave:* Lead aV_L was available for study in both the "first" electrocardiograms and the "one year" electrocardiograms in sixteen instances. In nine of the "first" electrocardiograms Q waves were present. The amplitude of the Q wave varied from 0.5 to 4.0 mm., and the duration varied from 0.01 to 0.06 sec. Q waves were present in nine of the "one year" electrocardiograms. The amplitude of the Q wave varied from 1.0 to 5.0 mm., and the duration varied from 0.02 to 0.06 sec. The Q wave had increased in five instances, decreased in two, and in two it was unchanged. The duration of the Q wave had increased in three instances, decreased in two, and in four it was unchanged.

2. *R wave:* In the "first" electrocardiograms the amplitude of the R wave varied from 1.0 to 12.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 1.0 to 16.0 mm. The amplitude of the R wave had increased in nine instances, decreased in four, and in three it was unchanged.

3. *T wave:* In the sixteen "first" electrocardiograms the T wave was inverted in thirteen instances and upright in three. In the "one year" electrocardiograms the T was inverted in eleven instances, upright in four, and isoelectric in one. Of the thirteen instances of inverted T waves in the "first" electrocardiograms the T remained negative in ten, became positive in two, and isoelectric in one in the "one year" electrocardiograms. The T was less negative in nine instances, more negative in four, and in three it was unchanged.

C. *Lead V_1.*—

1. *Q wave:* Lead V_1 was available in sixteen instances in both the "first" and "one year" electrocardiograms. A Q wave was present in this lead in the "first" electrocardiograms in the form of a QS pattern in thirteen instances.

TABLE III

	V_1				V_2				V_3			
	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.
"first"	0.06	9.0	0	3.0	0.07	18.0	0	5.0	0.07	11.0	0	3.0
"1 yr."	0.06	9.0	0	3.0	0.07	18.0	0	5.0	0.07	18.0	0	5.0
"first"	0.06	9.0	0	−1.0	0.08	7.0	0	−4.0	0.05	3.0	1.5	−3.0
"1 yr."	0.06	7.0	0	−1.0	0.06	4.0	0	−1.0	0.04	5.0	2.0	2.0
"first"	0.08	5.0	0	1.0	0.08	22.0	0	−3.0	0.08	20.0	0	−4.0
"1 yr."	0.08	9.0	0	2.0	0.08	17.0	0	4.0	0.08	14.0	0	−1.0
"first"	0.06	9.0	0	−0.5	0.06	17.0	0	−1.0	0.06	16.0	0	−2.0
"1 yr."	0.06	14.0	0	−1.0	0.06	20.0	0	−1.0	0.05	10.0	0	−1.0
"first"	0.07	7.0	0	2.0	0.07	17.0	0	−1.0	0.08	10.0	0	−1.0
"1 yr."	0.07	6.0	0	2.0	0.07	16.0	0	5.0	0.08	15.0	0	5.0
"first"	0.00	0	3.0	5.0	0.00	0	3.0	6.0	0.00	0	1.0	2.5
"1 yr."	0.00	0	3.0	2.0	0.00	0	3.0	2.0	0.00	0	2.0	2.0
"first"	0.08	7.0	0	1.0	0.08	17.0	0	−2.0	0.08	17.0	0	−2.0
"1 yr."	0.08	9.0	0	2.0	—	—	—	—	0.08	17.0	0	−1.0
"first"	0.08	13.0	0	−1.0	0.08	17.0	0	−6.0	0.07	12.0	0	−7.0
"1 yr."	0.08	12.0	0	2.0	0.08	14.0	0	−2.0	0.00	0	4.0	−4.0
"first"	0.07	15.0	0	−1.0	0.07	20.0	0	−1.0	0.07	12.0	0	−1.0
"1 yr."	0.07	10.0	0	2.0	0.08	6.0	0	−2.0	0.08	3.0	0	−3.0
"first"	0.08	8.0	0	−4.0	0.08	12.0	0	−9.0	0.08	10.0	0	−10.0
"1 yr."	0.08	4.0	0	−1.0	0.00	0	0.5	3.0	0.00	0	10.0	3.0
"first"	0.07	5.0	0	−0.5	0.08	20.0	0	−1.0	0.07	12.0	0	−2.0
"1 yr."	0.04	6.0	1.0	1.5	0.06	18.0	3.0	3.0	0.06	18.0	3.0	5.0
"first"	0.07	10.0	0	−2.0	0.07	19.0	0	−6.0	0.07	18.0	0	−9.0
"1 yr."	0.08	11.0	0	2.0	0.08	15.0	0	4.0	0.02	3.0	3.0	3−1.0
"first"	0.00	0	1.5	−2.0	0.07	10.0	0	−4.0	0.04	3.0	3.0	−5.0
"1 yr."	0.00	0	2.0	−2.0	0.07	14.0	0	−4.0	0.08	4.0	0	−4.0
"first"	0.06	9.0	0	1.0	0.06	23.0	0	−1.0	0.07	24.0	0	−2.0
"1 yr."	0.08	9.0	0	2.0	0.08	17.0	0	2.0	0.07	14.0	0	2.0
"first"	0.07	5.0	0	−1.5	0.09	23.0	0	2,−1.0	0.09	19.0	0	3.0
"1 yr."	0.05	7.0	0	0	0.09	15.0	0	1,−2.0	0.09	22.0	0	−1.0
"first"	0.00	0	2.0	2.0	0.02	2.0	9.0	−6.0	0.04	3.0	9.0	−5.0
"1 yr."	0.00	0	2.0	4.0	0.06	7.0	4.0	−2.0	0.08	9.0	4.0	−2.0
"first"					0.07	7.0	0	−3.0				
"1 yr."					0.08	7.0	0	−1.0				

The amplitude of the Q wave varied from 5.0 to 15.0 mm., and the duration varied from 0.06 to 0.08 sec. Q waves remained present in all thirteen instances in the "one year" electrocardiograms. The amplitude of the Q wave varied from 4.0 to 14.0 mm., and the duration from 0.04 to 0.08 sec. The amplitude of the Q wave had increased in six instances, decreased in five, and in two it was unchanged. The duration of the Q wave had increased in one instance, decreased in three, and in nine it was unchanged.

2. *R wave:* In three of the sixteen "first" electrocardiograms with Lead V_1, R waves were present. The amplitude of the R wave varied from 1.5 to 3.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 1.0 to 3.0 mm. The amplitude of the R wave had decreased in one instance and in two it was unchanged.

3. *T wave:* In nine of the sixteen "first" electrocardiograms the T wave was inverted, in seven upright. Of the nine instances with an inverted T wave

TABLE III—Cont'd

	V_4				V_5				V_6			
	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.	Q SEC.	Q MM.	R MM.	T MM.
"first"	0.07	4.0	0	—3.0	0.07	3.0	0	—3.0	0.06	2.0	0	—3.0
"1 yr."	0.07	4.0	0	—1.0	0.04	1.0	0.5	—2.0	0.03	1.0	2.0	—1.0
"first"	0.03	2.0	4.0	—2.0	0.03	2.0	4.0	—2.0	0.03	2.0	3.0	—1.0
"1 yr."	0 03	2.0	7.0	1.0	0.02	2.0	9.0	1.0	0.02	0.5	8.0	1.0
"first"	0.08	13.0	0	—5.0	0.08	13.0	0.0	—5.0	0.00	0	1.0	—5.0
"1 yr."	0.08	10.0	0	—2.0	0.00	0	5.0	—2.0	0.00	0	10.0	—2.0
"first"	0.06	12.0	0	—2.0	0.00	0	1.0	—2.0	0.00	0	2.0	—1.0
"1 yr."	0.00	0	1.0	—0.5	0.00	0	2.0	1.0	0.00	0	3.0	1.0
"first"	0.08	7.0	0	—1.0	0.08	6.0	0	—1.0	0.08	5.0	2.0	—2.0
"1 yr."	0.08	12.0	0	—3.0	0.08	8.0	2.0	—2.0	0.00	0	5.0	—2.0
"first"	0.03	2.0	2.0	—1.0	0.04	2.0	4.0	—1.5	0.04	1.0	3.0	—1.0
"1 yr."	0.03	2.0	2.0	—0.5	0.04	2.0	4.5	—0.5	0.04	1.0	4.0	0.5
"first"	0.08	13.0	0	—3.0	0.00	0	2.0	—3.0	0.00	0	2.0	—2.0
"1 yr."									0.00	0	2.0	—1.0
"first"	0.00	0	10.0	—4.0	0.00	0	11.0	—1.0	0.00	0	10.0	—1.0
"1 yr."	0.00	0	10.0	—3.0	0.00	0	8.0	±0.5	0.00	0	8.0	1.0
"first"	0.08	5.0	0	—6.0	0.00	0	8.0	—1.0	0.00	0	3.0	—1.0
"1 yr."	0.06	2.0	2.0	—2.0	0.00	0	5.0	—1.0	0.00	0	6.0	—1.0
"first"	0.00	0	4.0	—6.0	0.00	0	6.0	—1.0	0.00	0	5.0	—1.0
"1 yr."	0.00	0	11.0	3.0	0.00	0	10.0	4.0	0.00	0	10.0	4.0
"first"	0.07	11.0	0	—2.0	0.00	0	5.0	—2.0	0.00	0	9.0	—2.0
"1 yr."	0.03	9.0	6.0	—2.0	0.00	0	13.0	—5.0	0.00	0	9.0	—3.0
"first"	0.02	1.0	5.0	—6.0	0.00	0	6.0	—2.0	0.00	0	5.0	1.0
"1 yr."	0.00	0	12.0	1.0	0.00	0	11.0	0.5	0.00	0	7.0	0
"first"	0.00	0	16.0	—3.0	0.00	0	14.0	0	0.00	0	11.0	1.0
"1 yr."	0.00	0	18.0	—1.0	0.00	0	16.0	2.0	0.00	0	20.0	2.0
"first"	0.06	14.0	0	—2.0	0.00	0	2.5	—0.5	0.00	0	3.0	—1.0
"1 yr."	0.00	0	3.0	2,—1.0	0.00	0	5.0	—1,0.5	0.00	0	6.0	—1,0.5
"first"	0.09	12.0	0	3.0	0.09	4.0	0	2.0	0.03	1.0	2.0	1
"1 yr."	0.09	16.0	0	2,—3.0	0.09	18.0	0	2,—2.0	0.00	0	9.0	—2,—1
"first"	0.04	6.0	10.0	—5.0	0.04	6.0	6.0	—4.0	0.04	4.0	6.0	—2.0
"1 yr."	0.04	3.0	6.0	—2.0	0.06	4.0	3.0	—2.0	0.04	3.0	7.0	—2.0
"first"	0.06	15.0	0.0	—5.0								
"1 yr."	0.06	10.0	0.0	—1.0								

in the "first" electrocardiograms, the T wave remained negative in four, became upright in four, and isoelectric in one in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in ten instances, more negative in two, and in four it was unchanged.

D. *Lead V_2.*—

1. *Q wave:* Lead V_2 was available in sixteen instances in the "first" electrocardiograms and in fifteen instances in the "one year" electrocardiograms. In fifteen of the "first" electrocardiograms a Q wave was present. In fourteen of these there was a QS pattern. The amplitude of the Q wave varied from 2.0 to 23.0 mm., and the duration from 0.02 to 0.09 sec. Q waves were present in the "one year" electrocardiograms in thirteen instances. In twelve of these there was a QS pattern. The amplitude of the Q wave varied from 1.0 to 22.0 mm., and the duration from 0.01 to 0.07 sec. The amplitude of the Q wave had increased in three instances, decreased in nine, and in two it was unchanged.

The duration of the Q wave had increased in four instances, decreased in two, and in eight it was unchanged.

2. *R wave:* In two of the sixteen "first" electrocardiograms with Lead V_2, R waves were present. The amplitude of the R wave was 3.0 to 9.0 mm. In the "one year" electrocardiograms the amplitude of the R wave had decreased in one instance and in the other it was unchanged. There were R waves present in four instances in the "one year" electrocardiograms. The amplitude of the R wave varied from 0.5 to 4.0 mm.

3. *T wave:* In thirteen of the sixteen "first" electrocardiograms the T wave was inverted, in two upright, and in one diphasic. Of the thirteen instances with an inverted T wave in the "first" electrocardiograms, the T remained negative in six, became upright in six, and this lead was not available in one. The T wave in the "one year" electrocardiograms was less negative in ten instances, more negative in one, and in four it was unchanged.

E. *Lead V_3.*—

1. *Q wave:* Lead V_3 was available in sixteen instances in both the "first" and the "one year" electrocardiograms. In fifteen of the "first" electrocardiograms there was a Q wave present. In twelve of these there was a QS pattern. The amplitude of the Q wave varied from 3.0 to 13.0 mm., and the duration from 0.04 to 0.09 sec. Q waves were present in the "one year" electrocardiograms in thirteen instances. There was a QS pattern in ten of these. The amplitude of the Q wave varied from 3.0 to 12.0 mm., and the duration from 0.02 to 0.09 sec. The amplitude of the Q wave had increased in seven instances, decreased in seven, and in one it was unchanged. The duration of the Q wave had increased in three instances, decreased in six, and in six it was unchanged.

2. *R wave:* In four of the sixteen "first" electrocardiograms with Lead V_3, R waves were present. The amplitude of the R wave varied from 1.5 to 9.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 2.0 to 10.0 mm. The amplitude of the R wave had increased in two instances, and decreased in two instances.

3. *T wave:* In thirteen of the sixteen "first" electrocardiograms the T wave was inverted, in three upright. Of the thirteen instances with an inverted T wave in the "first" electrocardiograms, the T wave remained negative in seven, became upright in five, and diphasic in one in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in thirteen instances, and more negative in three instances.

F. *Lead V_4.*—

1. *Q wave:* Lead V_4 was available in seventeen instances in the "first" electrocardiograms and in sixteen instances in the "one year" electrocardiograms. In fourteen of the "first" electrocardiograms a Q wave was present. In ten of these there was a QS pattern. The amplitude of the Q wave varied from 1.0 to 14.0 mm., and the duration from 0.02 to 0.09 sec. Q waves were present in the "one year" electrocardiograms in ten instances. In five of these there was a QS pattern. The amplitude of the Q varied from 2.0 to 16.0 mm., and the

duration from 0.03 to 0.09 sec. The amplitude of the Q wave had increased in three instances, decreased in seven, and in three it was unchanged. The duration of the Q wave had increased in one instance, decreased in four, and in seven it was unchanged.

2. *R wave:* In seven of the seventeen "first" electrocardiograms with Lead V_4, R waves were present. The amplitude of the R wave varied from 2.0 to 16.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 1.0 to 18.0 mm. The amplitude of the R wave had increased in four instances, decreased in one, and in two it was unchanged.

3. *T wave:* In sixteen of the seventeen "first" electrocardiograms the T wave was inverted, in one upright. Of the sixteen instances with an inverted T wave in the "first" electrocardiograms, the T wave remained negative in eleven, became upright in two, and diphasic in two in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in thirteen instances, more negative in two, and in one it was unchanged.

G. *Lead V_5.*—

1. *Q wave:* Lead V_5 was available in sixteen instances in the "first" electrocardiograms and in fifteen instances in the "one year" electrocardiograms. In seven of the "first" electrocardiograms a Q wave was present. In four of these there was a QS pattern. The amplitude of the Q wave varied from 2.0 to 13.0 mm., and the duration from 0.03 to 0.09 sec. Q waves were present in the "one year" electrocardiograms in six instances. In one of these there was a QS pattern. The amplitude of the Q wave varied from 1.0 to 18.0 mm., and the duration from 0.02 to 0.09 sec. The amplitude of the Q wave had increased in two instances, decreased in three, and in two it was unchanged. The duration of the Q wave had decreased in four instances, and in three it was unchanged.

2. *R wave:* In twelve of the sixteen "first" electrocardiograms with Lead V_5, R waves were present. The amplitude of the R wave varied from 1.0 to 14.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 0.5 to 16.0 mm. The amplitude of the R had increased in seven instances, decreased in four, and in one it was unchanged.

3. *T wave:* In fourteen of the sixteen "first" electrocardiograms the T wave was inverted, in one upright, and in one isoelectric. Of the fourteen instances, with an inverted T wave in the "first" electrocardiograms, the T wave remained negative in seven, became upright in four, and diphasic in two in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms became less negative in eleven instances, and more negative in three.

H. *Lead V_6.*—

1. *Q wave:* Lead V_6 was available in sixteen instances in both the "first" and "one year" electrocardiograms. In six of the "first" electrocardiograms a Q wave was present. In two of these there was a QS pattern. The amplitude of the Q wave varied from 1.0 to 5.0 mm., and the duration from 0.03 to 0.08 sec. Q waves were present in the "one year" electrocardiograms in four instances. The amplitude of the Q wave varied from 0.5 to 3.0 mm., and the

duration from 0.02 to 0.04 sec. The amplitude of the Q wave had decreased in five instances, and in one it was unchanged. The duration of the Q wave had decreased in four instances, and in two it was unchanged.

2. *R wave:* In fifteen of the sixteen "first" electrocardiograms, R waves were present. The amplitude of the R wave varied from 1.0 to 11.0 mm. In the "one year" electrocardiograms the amplitude of the R wave varied from 2.0 to 20.0 mm. The amplitude of the R wave had increased in twelve instances, decreased in one, and in one it was unchanged.

3. *T wave:* In thirteen of the sixteen "first" electrocardiograms the T wave was inverted, in three upright. Of the thirteen instances with an inverted T wave in the "first" electrocardiograms, the T remained negative in seven, became upright in five, and diphasic in one in the "one year" electrocardiograms. The T wave in the "one year" electrocardiograms was less negative in ten instances, more negative in three, and in three it was unchanged.

RS-T SEGMENT

The RS-T segment was isoelectric in all instances in the "first" and "one year" electrocardiograms in Lead I and aV_L. The RS-T segment was elevated in the right precordial leads in the "first" tracings in eleven instances. One patient was receiving digitalis and one quinidine. The RS-T segment remained elevated in eleven instances in the "one year" electrocardiograms. The greatest elevation in the "first" tracings was 3.0 mm. The greatest elevation in the "one year" tracings was 2.0 mm. The RS-T elevation decreased in five instances and increased in five. In the left precordial leads the RS-T segment was elevated in four instances in the "first" tracings. In the "one year" tracings the RS-T segment was elevated in five instances. The RS-T elevation increased in two instances, and decreased in one.

QRS DURATION

In the "first" electrocardiograms the longest QRS was 0.09 sec., shortest 0.06 sec., average 0.08 sec. In the "one year" tracings the longest QRS was 0.09 sec., shortest 0.05 sec., average 0.07 sec. The QRS duration increased in three instances, decreased in six, and in fifteen it was unchanged.

Q-T_c INTERVAL

In the "first" electrocardiograms the longest Q-T_c was 0.49 sec., shortest 0.34 sec., average 0.42 sec. In the "one year" electrocardiograms the longest Q-T_c was 0.45 sec., shortest 0.34 sec., average 0.40 sec. The Q-T_c duration increased in six instances, decreased in fifteen, and in three it was unchanged. The average increase was 0.02 sec. The average decrease was 0.04 sec.

DISCUSSION

Several findings in the above analysis of electrocardiograms taken one year after acute myocardial infarction appear to have clinical significance.

In almost all instances if the "first" electrocardiograms had an initial negative deflection in the signal leads, this Q wave was still present in the "one year"

electrocardiogram. It might get smaller, larger, or stay unchanged; only rarely did the larger Q waves, 2.0 mm. or more and 0.04 sec. or more in the "first" electrocardiograms, decrease below these values in the "one year" electrocardiograms. This observation indicates correlation between the size of the initial dead zone vector and its persistence in the records one year later.

The T wave tended to revert toward normal substantially more than did the Q wave in the "one year" electrocardiograms. In the large majority of the latter tracings T in the signal leads had increased in positivity.

Previously we have reported on characteristic changes in the right precordial lead in patients with acute myocardial infarction of the posterior wall.[9] These consisted of increases in amplitude of R and a more striking increase in positivity of T resulting in upright T waves in this lead, in contrast to the negative T wave here in acute cor pulmonale. However, no long term follow-up was made. It is of interest to note that in the present series in all but one instance these findings persisted in the "one year" electrocardiograms.

The above electrocardiographic findings appear in conformity with the expected evolution of the pathologic changes in acute myocardial infarction. It seems unlikely that an area of necrosis with replacement by fibrous scar tissue and loss of electrical potentials would have a return of its electrical activity. Its absence represented by the Q wave therefore should be permanent. If shrinkage or stretching of the myocardial scar does occur after the first few months, this could result in corresponding changes in magnitude of the dead zone vector and the Q wave, as observed. However, areas of injury or ischemia of the myocardium might well return to normal, with complete disappearance of their electrocardiographic manifestations. All these changes were better reflected in the precordial leads apparently due to the proximity of the electrode to the cardiac area involved.

In a review of the complete electrocardiograms in these fifty-one patients one year following myocardial infarction, we have been able to classify only one tracing as within normal limits and only three tracings as almost normal. This is at variance with impressions and statements gathered from the reports in the literature which would seem to indicate a much greater incidence of return to normal. An exception is the very recent report of William Evans, who, utilizing CR_1 to CR_7, emphasized the immutability of the electrocardiogram of myocardial infarction. Although nearly one-half (23 out of 51) of our "one year" electrocardiograms showed some restitution toward normal, chiefly on the basis of T wave changes, these records still remained definitely abnormal. In fourteen instances the "one year" electrocardiograms showed no significant change from the "first" electrocardiograms. Finally, a completely normal 12-lead electrocardiogram would be strong evidence against the presence of an acute myocardial infarction, anterior or posterior wall type, one year previously.

SUMMARY AND CONCLUSIONS

1. The electrocardiograms of fifty-one patients with acute myocardial infarction were analyzed at the time of their discharge from the hospital and again one year later.

2. Behavior of the QRS complex, the Q-T interval, the RS-T segment and the T wave is described. Serial changes noted in the electrocardiograms one year following myocardial infarction are reported.

3. In only one of fifty-one instances of acute myocardial infarction did the 12-lead electrocardiogram with typical changes return to normal one year later; a completely normal 12-lead electrocardiogram is therefore strong evidence against the presence of an acute myocardial infarction of the classical anterior or posterior wall type, one year previously.

SUMMARIO IN INTERLINGUA

1. Le electrocardiogrammas de 51 patientes con acute infarcimento myocardial esseva analysate al tempore de lor dimittimento ab le hospital e de novo un anno plus tarde.

2. Es describite le conducta del complexo QRS, del intervallo Q-T, del segmento RS-T, e del unda T. Es reportate alterationes serial notate in le electrocardiogrammas un anno post infarcimento myocardial.

3. Esseva trovate in iste serie de 51 casos de acute infarcimento myocardial non plus que un sol caso in que le electrocardiogramma a 12 derivationes exhibiente alterationes typic retornava al norma intra un anno. Ergo un completemente normal electrocardiogramma a 12 derivationes es un forte indication contra le presentia, un anno retro, de un acute infarcimento myocardial del typo classic involvente le pariete anterior o posterior.

We gratefully acknowledge the cooperation of the members of the medical staff of Beth Israel Hospital who have graciously made electrocardiograms of their private patients available to us for this study.

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PREMATURE BEATS IN ATRIOVENTRICULAR RHYTHM

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THE basic laws which determine disturbance of rhythm by premature beats were laid down by Marey,[1] Englemann,[2] Cushny and Mathews,[3] Cushny,[4] and Wenckebach.[5] Disturbance of the dominant rhythm depends on invasion of the pacemaker by the premature excitation. If the abnormal stimulus is not transmitted to the pacemaker, or fails to reach it early enough to discharge it prematurely, the basic rhythm remains undisturbed. The heart chamber which has been activated by the premature excitation is usually in a refractory state, when the regular stimulus arrives, and fails to respond. The following impulse which originates in the normal pacemaker, again causes a contraction of the heart. The period after the premature beat, the "returning cycle,"* is that much longer than a normal period, as the cycle before the premature beat is shortened. This is to say, the returning cycle is of compensatory length.[1-3] Most of the premature beats of ventricular origin fit into this pattern.

Premature excitations which originate in the atrium as a rule travel to the S-A node and cause its premature discharge. Thus a shift in the dominant rhythm is produced. After the discharge it takes a normal period until a new stimulus is produced by the regular pacemaker. The returning cycle, then, is of less than compensatory length, though it is usually longer than a normal period. The excess was attributed by Wenckebach[5] to the time required for the abnormal excitation to travel to the dominant pacemaker. In some instances, especially when the premature beat falls very early in diastole, the excess in length of the returning cycle is distinctly longer than is explained by the travel time. It is therefore postulated that the premature excitation has an inhibiting effect[4] which retards either the formation of the next ordinary impulse or the response of a hypodynamic heart.[4,8,9]

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*For descriptive purposes it is convenient to use a certain terminology.[6,7] The normal beats and cycles which precede the premature beat are referred to as "initial" beats and cycles. The shortened period before the premature beat is called the "extrasystolic cycle" or "coupling." The period which follows the premature beat is the "returning cycle." Coupling plus the returning cycle form the "conjoined cycles." The normal beats which follow the premature contraction are named "restored beats" and the intervals between them the "restored cycles". Similarly the A-V conduction time can be qualified by the adjective attached to the cycle which it terminates.

Some atrial premature beats are followed by a compensatory pause. This occurs when the abnormal impulse falls late in the diastole and is therefore unable to discharge prematurely the dominant pacemaker; or compensation may be simulated by fortuitous prolongation of the cycle of the dominant rhythm.[6] Premature atrial beats have often a longer A-V conduction time than regular excitations. The earlier in diastole the premature excitation falls the longer, as a rule, is its A-V conduction time.

The laws governing disturbance of rhythm by premature beats were originally derived from hearts beating in S-A rhythm. They were later shown in the experimental animal to apply equally to A-V rhythm.[6,8,10] However, when the A-V node is the dominant pacemaker, disturbance in the conductivity of the junctional tissues may produce striking changes in the sequence of atrial and ventricular contractions.[10,11] Such transient changes which follow premature beats were analyzed in the experimental animal by Scherf and Shookhoff.[10] Few clinical observations of premature beats occurring in A-V rhythm are on record.[12-14] This report deals with premature beats of ventricular and supraventricular type observed in man in the presence of A-V rhythm of various origin.

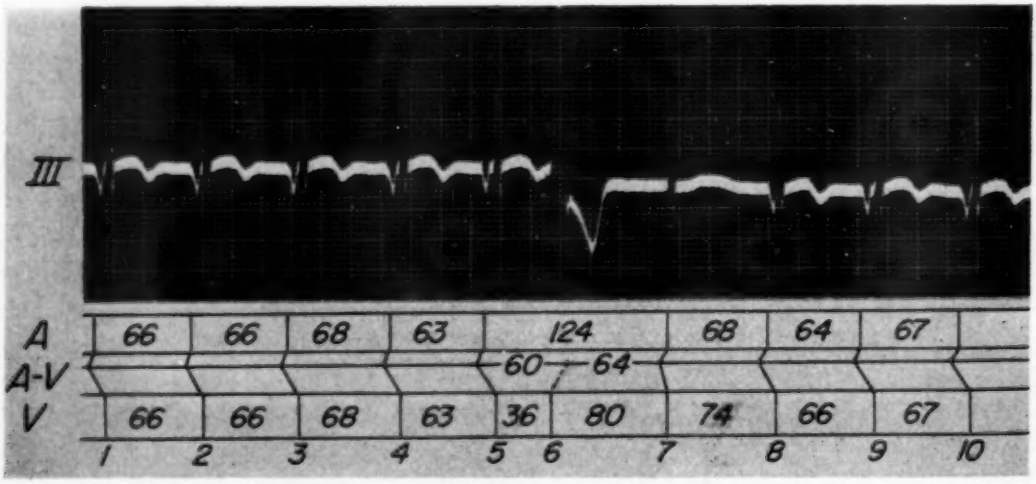

Fig. 1.—Case 1. Lead III. Inverted P waves precede the QRS complexes by 0.08 sec., indicating upper A-V rhythm. The sixth beat is a premature ventricular contraction. The following beat shows no P wave, and the direction of the T deflection is upright. The second postextrasystolic beat shows an inverted P wave which precedes the QRS complex by 0.05 sec. The third beat presents the same As-Vs sequence as the initial contractions. (The figures in this and the following tracings indicate hundredths of a second.)

1. PREMATURE VENTRICULAR BEATS IN UPPER A-V NODAL RHYTHM

CASE 1.—H.B. Fig. 1, Lead III. The first 5 beats have inverted P waves which precede the ventricular complexes by 0.08 sec. These features suggest a rhythm originating in the upper portion of the A-V node. The sixth beat is premature and comes apparently from the ventricle. It is not discernable whether or not a premature P wave is hidden in its large ventricular deflections. The following 2 beats show striking changes in the As-Vs sequence. The first is not preceded by a P wave and its T deflection is upright. The second beat after the extrasystole shows an inverted P wave which precedes the ventricular complex by 0.05 sec. In the third postextrasystolic beat the initial As-Vs sequence is restored. It is significant that the length of the restored cycles does not appreciably differ from that of the initial cycles.

A clinical tracing presenting a similar disturbance was reported by Edens,[14] who attributed the changed As-Vs relationship after the premature beat to wandering of the pacemaker. Scherf and Shookhoff[10] drew attention to an identical phenomenon which they observed in the experimental animal, when premature beats of ventricular origin were conducted retrogradely to the atrium. Unlike Edens, the authors assumed that, following invasion of the A-V center by the premature ventricular excitation, the initial rhythm was restored, as shown by return of the initial cycle length. The temporary change in the As-Vs sequence after the extrasystole was attributed to a variation in A-V conduction which resulted from retrograde transmission of the premature ventricular excitation.

The diagram below the tracing in Fig. 1 illustrates the interpretation which was given to the postextrasystolic phenomenon by Scherf and Shookhoff. The authors pointed out that in the first restored beat, atrium and ventricle contract simultaneously, hence the P wave is hidden in the QRS complex. If their interpretation is applied to this case, the beginning of P approximately coincides with the onset of R, and the length of the conjoined cycles measures 1.24 sec., which is less than two initial cycles. It can be therefore concluded that the A-V nodal center was invaded by the premature excitation. The next regular impulse is released after a normal or slightly prolonged cycle and reaches the atrium at the usual transmission rate. Conduction to the ventricle, however, is shortened because retrograde transmission of the premature ventricular excitation and possibly also retardation of the following regular beat provide a prolonged recovery time for the junctional tissues distal to the A-V pacemaker. Therefore the first postextrasystolic impulse reaches the ventricle and atrium at the same time, and the P wave merges with the QRS complex. In the following beat the ventricular contraction falls somewhat later than the atrial systole, and in the third beat the initial As-Vs sequence is restored. The first restored cycle measures 0.68 sec. in the atria and 0.74 sec. in the ventricles. The difference in length is due to accelerated conduction of the first postextrasystolic A-V nodal excitation to the ventricle. In as much as in the following beats conduction from the A-V pacemaker to the ventricles slows down again, the difference in the duration of the restored atrial and ventricular cycles is abolished.

The reversal in the direction of the T wave in the first restored beat represents one of the changes which frequently follow premature contractions.[16]

2. PREMATURE VENTRICULAR BEATS IN LOWER A-V NODAL RHYTHM

Case 2.—J.S. Fig. 2,*A*, Lead III. Inverted P waves follow the QRS complexes after intervals ranging from 0.12 to 0.13 sec. These features are suggestive of lower A-V nodal rhythm. The duration of the basic cycle varies from 0.62 to 0.67 sec. The A-V rhythm is disturbed by three premature beats of ventricular origin; their couplings are 0.40, 0.50, and 0.54 sec., respectively. The conjoined cycles measure 1.16, 1.24, and 1.27 sec. respectively, that is, less than two initial cycles. The returning cycles, therefore, are noncompensatory, indicating that the A-V center was disturbed by retrograde transmission of the premature ventricular excitation. In Lead III no inverted P waves are distinctly outlined in the premature ventricular beats. In Lead CF_4, however (Fig. 2,*B*), an upright P wave is recognizable which follows the premature QRS complex after an interval of 0.25 sec. It is premature, its coupling being 0.56 sec., while the length of the initial cycles ranges from 0.62 to 0.64 sec. The shape of the premature P wave is identical with that of the regular A-V beats. Hence, it can be concluded that the atrium has been activated by the retrogradely conducted premature excitation.

The returning atrial cycle measures 0.60 sec. (Fig. 2,*B*). It is shorter than the initial cycles, presumably because conduction of the premature excitation from the A-V center to the atrium is slower than in the regular beats. The returning cycle in the ventricle measures 0.72 sec. It is longer than the returning atrial cycle by the difference of the Vs-As intervals of the premature contraction and the first restored beat.

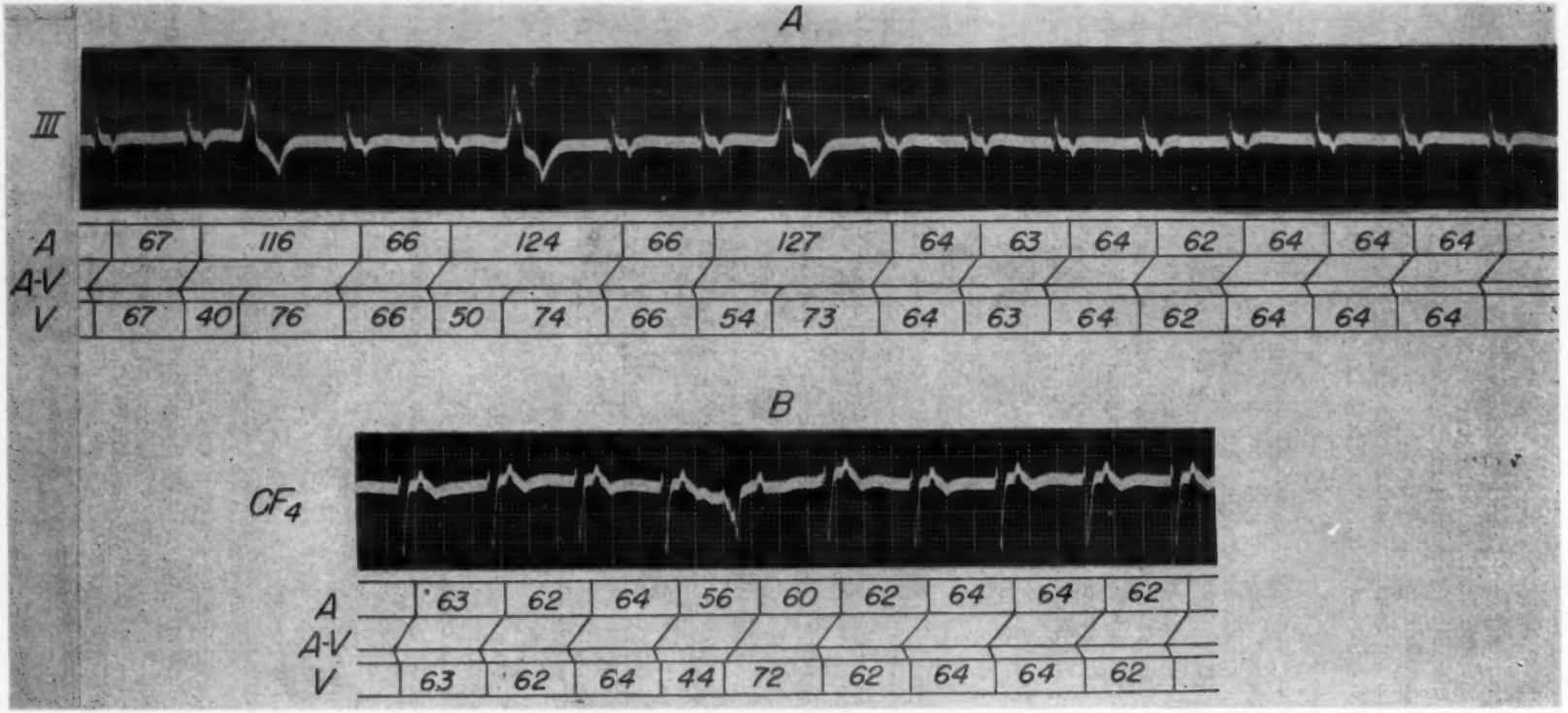

Fig. 2.—Case 2. *A*, **Lead III.** Inverted P waves follow the QRS complexes after intervals measuring 0.12 to 0.13 sec. This is suggestive of lower A-V rhythm. There are three premature beats of ventricular origin with varying coupling. The basic cycle measures 0.62 to 0.67 sec. The conjoined cycles are less than two initial cycles, hence the pauses after the premature beats are noncompensatory. Atrial waves are not distinctly recognizable in the premature ventricular beats.

B, **Lead CF_4.** The QRS complexes are regularly followed by upright P waves, the R-P interval measuring 0.14 to 0.15 sec. An identical P wave follows a premature ventricular beat after an interval of 0.25 sec. This indicates that the atrium has been activated by the premature ventricular excitation. The conjoined cycles measure 1.16 sec., less than two initial cycles. The returning cycle measures 0.60 sec. in the atria, and 0.72 sec. in the ventricles.

3. LOWER A-V NODAL RHYTHM WITH UPRIGHT P WAVES IN LEADS II AND III, INTERRUPTED BY PREMATURE BEATS OF VENTRICULAR AND ATRIAL ORIGIN

CASE 3.—J.M. Fig. 3,*A* presents a fairly regular bradycardia of supraventricular origin. The rate is 33 per minute. No P waves are seen in front of the ventricular beats, but each QRS complex is followed after an interval of 0.16 sec. by an atrial wave which is inverted in Lead I, upright in Leads II and III. Such a sequence of ventricular and atrial contractions is usually associated with lower A-V rhythm. Upright P waves were observed in ano-esophageal leads, which are comparable to Lead III, in experimentally produced A-V rhythm. The upright direction of P was attributed to abnormal conduction in the atrium.[15]

Fig. 3,*B* from the same patient, shows the same type of rhythm at a rate of 83 per minute. The length of the basic cycle is 0.72 to 0.74 sec. The R-P interval measures 0.13 to 0.14 sec. The

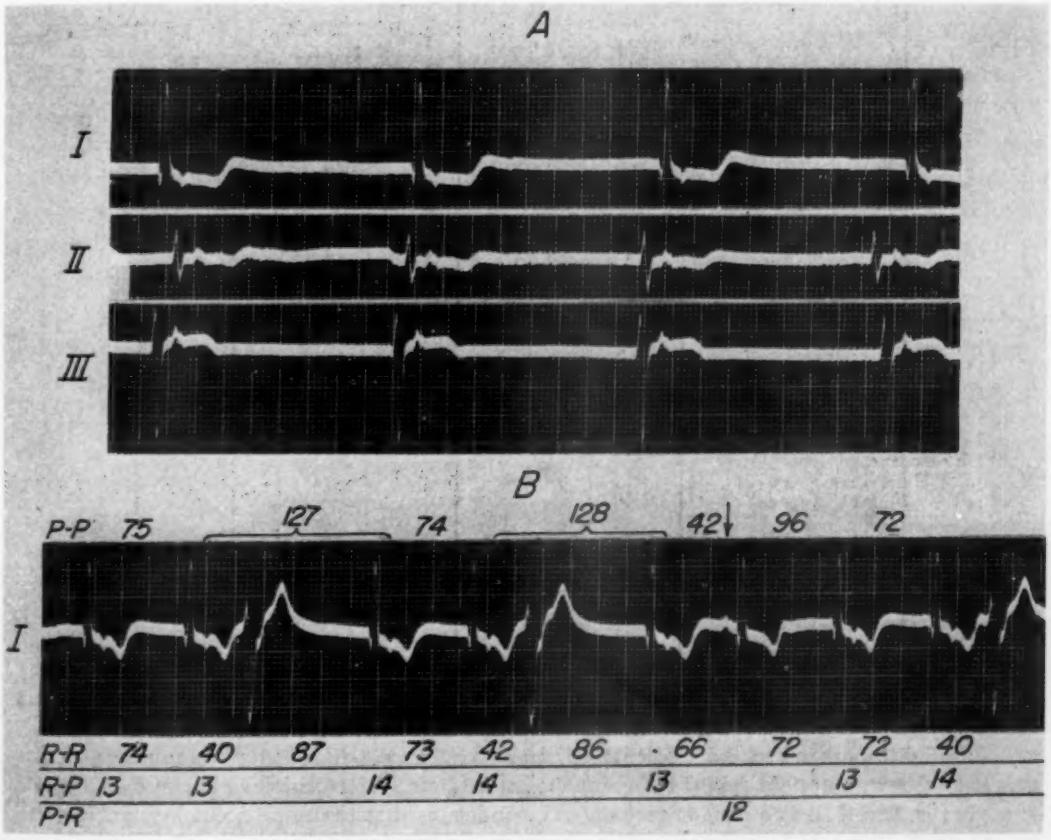

Fig. 3.—Case 3. *A*, **There is a fairly regular bradycardia, the shape of the ventricular beats suggesting supraventricular origin. The QRS complexes are followed regularly, after an interval of 0.16 sec., by P waves which are inverted in Lead I, upright in Leads II and III. The sequence of ventricular and atrial contractions suggests lower A-V rhythm.**

B, **Lead I. Same type of basic rhythm as in Fig. 2,*A* but much faster. Three premature beats of ventricular origin are present. The pauses after the premature beats are noncompensatory. The conjoined cycles measure 1.27 and 1.28 sec., respectively, that is, less than two initial cycles. The eighth beat (↓) is apparently a premature atrial contraction. An upright P wave precedes the QRS complex by 0.12 sec. The returning cycle is noncompensatory. The conjoined cycles measure 1.38 sec., and the length of the preceding basic cycle is 0.74 sec. The returning ventricular cycle measures 0.72 sec., the same as the restored ventricular cycle.**

third, the sixth and the last beat are premature ventricular contractions. It is uncertain whether or not they contain P waves. The coupling is 0.40 to 0.42 sec. The conjoined cycles measure 1.27 and 1.28 sec., respectively, which is less than two regular cycles. This indicates that the A-V pacemaker was invaded by the premature ventricular excitations. The returning ventricular cycles are longer than the initial ventricular cycles, the difference being made up by the time required for the premature ventricular excitations to travel to the A-V pacemaker and the conduction time of the returning beat from the A-V center to the ventricle. Twenty-four ventricular beats were recorded in Case 3. Table I indicates the length of the returning cycles which is compared with that of the initial cycles and correlated to the couplings. The difference in the duration of the returning and initial cycles ranges from 0.08 to 0.18 sec. Such great differences, with the coupling varying only slightly, suggest that variations in the rate of discharge of the A-V center might play a significant part.

TABLE I. PREMATURE VENTRICULAR BEATS IN CASE 3

NO. OF PREMATURE BEAT	LENGTH OF COUPLING	DURATION OF RETURNING CYCLE	DURATION OF INITIAL CYCLE	DIFFERENCE IN THE LENGTH OF THE RETURNING AND INITIAL CYCLES
1	0.40	0.87	0.75	0.12
2	0.40	0.88	0.76	0.12
3	0.41	0.86	0.70	0.16
4	0.41	0.93	0.79	0.14
5	0.41	0.90	0.76	0.14
6	0.42	0.86	0.74	0.12
7	0.42	0.92	0.82	0.10
8	0.42	0.90	0.76	0.14
9	0.42	0.94	0.79	0.15
10	0.42	0.91	0.76	0.15
11	0.42	0.88	0.76	0.12
12	0.42	0.88	0.78	0.10
13	0.42	0.84	0.76	0.08
14	0.42	0.83	0.73	0.10
15	0.43	0.94	0.76	0.18
16	0.43	0.90	0.82	0.08
17	0.43	0.88	0.76	0.12
18	0.44	0.89	0.72	0.17
19	0.44	0.82	0.73	0.09
20	0.44	0.84	0.75	0.09
21	0.44	0.84	0.75	0.09
22	0.44	0.88	0.74	0.14
23	0.44	0.87	0.76	0.11
24	0.44	0.91	0.78	0.13

The eighth beat in Fig. 3,*B* (indicated by an arrow) is premature and of the supraventricular type. It shows an upright P and a P-R interval of 0.12 sec. The conjoined cycles measure 1.38 sec., that is, less than two regular periods. This indicates that the A-V pacemaker was invaded by the premature atrial excitation. The returning ventricular cycle, which reflects the "internodal time" measures 0.72 sec.; it is equal in length with the restored cycle and measures slightly less than the regular cycles in the first half of the tracing. The returning R-P interval measures 0.13 sec.; it has the same length as the Vs-As interval in the first two regular beats of the tracing.

COMMENT

Disturbance of the A-V rhythm by premature beats was extensively investigated in the experimental animal.[6,8,10] In comparing clinical observations with experience derived from the experimental animal, it is well to bear in mind

differences in basic conditions which may modify the effect of premature beats. In the experimental animal, section of the vagus nerve eliminates a factor of nerve tone. Furthermore conditions favoring disturbance of conduction were deliberately produced by forcing several premature beats in rapid sequence or by adminstration of quinine.[10] Long exposure of the heart in the experiment or the action of drugs renders the heart hypodynamic and may retard the response to regular impulses following premature beats.[8,9] These factors may account for some differences in the reaction of the heart to premature beats in the experimental animal and in clinical observations.

In the experimental animal the majority of premature beats in the presence of A-V rhythm are followed by noncompensatory pauses.[6,8] This is especially true of premature beats of atrial origin.[6] Ventricular extrasystoles frequently cause an atrial response and a shift of the basic A-V rhythm. Only when the premature atrial or ventricular excitation is blocked or arrives too late to disturb the pacemaker, full compensation of the premature beat takes place. Sometimes, however, even when premature beats arrive early in diastole, compensation is simulated by their retarding effect on the basic rhythm.[6,8]

In the three cases of this report a total of 16 atrial and 34 ventricular premature beats was observed in the presence of A-V rhythm. In every instance the returning cycle was noncompensatory, suggesting invasion of the dominant pacemaker. It is usually difficult to prove retrograde activation of the atrium by premature ventricular beats, because P waves are not readily recognizable in the large ventricular deflections. In Case 2, however, the finding of a premature P wave indicated clearly that the atrium was activated by the abnormal ventricular excitation. In the presence of S-A rhythm, retrograde activation of the atrium by premature ventricular beats is thought to be a rare event.[7,17] A case of lower A-V nodal rhythm of long standing was reported, in which ventricular premature beats were almost invariably conducted to the atrium.[18] This was attributed to "Bahnung," that is, preparation of the junctional tissues for retrograde conduction by frequent transmission of A-V nodal impulses. The present observations seem to support this view. Recently Kistin and Landowne, on the basis of experience derived from the use of esophageal leads, suggested that activation of the atrium by premature ventricular excitations was more common than it was thought hitherto.[19]

The length of the returning cycle differs for the atrium and ventricle according to the origin of the premature beats. When the premature excitation originates in the atrium the returning cycle in the ventricle is approximately a measure of the time which elapses between the invasion of the A-V center and the formation of the next ordinary impulse. It represents exactly the "internodal interval" when conduction from the A-V node to the ventricle is at the same rate for the premature and restored beats.[6] In the experimental animal the returning ventricular cycle after premature atrial beats is generally longer, and only exceptionally shorter than the initial cycle, the variations in length measuring rarely more than a few thousandths of a second. Prolongation is likely to be associated with greater prematurity. The returning cycle is longer in the atrium than in the ventricle by the difference of the extrasystolic and returning As-Vs intervals.[6]

Sixteen premature atrial beats with constant coupling were observed in Case 3. Since these beats followed closely either each other or premature ventricular contractions, their returning cycles could not be compared with initial cycles. Only in nine instances was it possible to compare the length of the returning ventricular cycles with that of restored cycles. The measures were identical for both cycles in five extrasystoles. In four instances the returning cycle was slightly shorter, the difference varying from 0.01 to 0.03 sec. This could be due either to a spontaneous variation in the rate of the dominant rhythm or to a delay in the conduction of the premature excitation from the A-V pacemaker to the ventricle. Scherf and Shookhoff[10] observed in experimentally produced A-V rhythm following premature atrial beats a temporary advance of the P wave, which they attributed to impaired conductivity of His's bundle. We have never seen in our clinical cases a similar disturbance in the As-Vs sequence following premature beats of atrial origin.

When premature beats arise in the ventricle, it is the returning cycle in the atrium which reflects the "internodal interval," providing that conduction from the A-V pacemaker to the atrium takes place at the same rate for the premature and restored contractions. Lewis and White observed in the experimental animal that, contrary to expectation, the returning cycle in the atria was prolonged by a few hundredths or thousandths of a second rather than shortened. In our Case 2 (Fig. 2,*B*), in which the returning atrial cycle could be measured, it was shorter by 0.04 sec. than the initial cycle. This difference is readily explained by delayed conduction of the premature ventricular excitation from the A-V pacemaker to the atrium.

In premature beats of ventricular origin the returning cycle in the ventricle is longer than that in the atrium by the difference of the extrasystolic and returning Vs-As intervals. Since in most of the extrasystoles which we observed atrial waves were not recognizable, and therefore the returning atrial cycles could not be measured, comparison was made of the returning and initial ventricular cycles. When the "internodal interval" is constant, the returning ventricular cycle is longer than the initial cycle by the conduction time of the premature impulse from the ventricle to the A-V pacemaker plus the time required for the regular impulse to reach the ventricle. In Case 2, in which the couplings of the premature ventricular beats vary considerably, the differences in length of the returning and initial ventricular cycles range from 0.08 to 0.10 sec. These variations could be conceivably explained by differences in the length of the coupling, the premature beats with shorter coupling having generally a longer Vs-As conduction time and therefore longer returning cycles. However, this explanation does not hold true for Case 3 in which the couplings of 24 premature ventricular beats vary only from 0.40 to 0.44 sec. Yet the differences in the length of the returning and initial ventricular cycles range from 0.08 to 0.18 sec. (Table I). Such great variations, which bear no relationship to the coupling, might be explained by changes in nerve tone causing variations in the rate of discharge of the A-V pacemaker.

In experimentally produced rhythm striking changes in the As-Vs sequence were observed following premature beats of ventricular origin.[10] They were attributed to variations in the conductivity primarily of His's bundle resulting

from retrograde transmission of the premature ventricular excitation and from retardation of the restored beat. The effect varies in upper and lower A-V rhythms, and furthermore depends on whether or not the premature ventricular excitation invades the A-V pacemaker. In the presence of upper A-V rhythm, premature ventricular excitations which disturb the basic rhythm are sometimes followed by temporary advance of the ventricular contraction, so that the P wave of the restored beat merges with the QRS complex. This phenomenon was explained by improved conductivity of the junctional tissues distal to the A-V pacemaker, because of prolonged recovery time following retrograde transmission of the premature ventricular excitation. This pattern of postextrasystolic disturbance is demonstrated in Fig. 1. In the experimental animal the phenomenon was never observed when the premature ventricular excitation did not reach the pacemaker.

Conditions are reverse when lower A-V rhythm is present and the premature ventricular excitation penetrates only for a short distance into the junctional tissues without reaching the A-V pacemaker.[10] The regular impulse which follows finds conductivity impaired in that part of the bundle which had been just passed by the ventricular impulse, and arrives late in the ventricle. Therefore, the P wave of the restored beat may temporarily advance in front of the QRS complex. If however, the premature ventricular excitation is able to reach and invade the A-V pacemaker, conductivity in the junctional tissues remains unimpaired and the Vs-As sequence of the restored beats is the same as in the initial contractions. The latter conditions are illustrated in Figs. 2 and 3.

In our Case 3, the sequence of ventricular and atrial contractions indicates lower A-V rhythm, yet the P waves are upright in Leads II and III. It is generally thought that inverted P waves in Leads II and III are required for the diagnosis of A-V rhythm.[7,17] McGuire and Rosenberger reported a case of A-V extrasystoles which were characterized by upright P waves and an abnormally short P-R interval.[20] In the experimental animal inversion of the P waves has been observed in the presence of S-A rhythm when intra-atrial conduction was disturbed by ligation of the muscular fascicle connecting the S-A node with the left atrium.[21] On the other hand, in the presence of A-V rhythm, disturbed conduction from the A-V node to the atrium may change the pathway of the excitation in such a way so as to produce upright P waves.[15] Scherf and Shookhoff were able, in experimentally produced A-V rhythm, to change the shape and direction of the P waves by the effect of quinine or of several premature forced beats in succession, which are known to cause disturbance of conductivity.[15] The authors pointed out that so far, only in the dog, upright P waves were observed in association with A-V rhythm. The case illustrated in Fig. 3 which presents the Vs-As sequence of lower A-V rhythm indicates that A-V rhythm occurring in man may be occasionally associated with upright P waves in Leads II and II.

SUMMARY

Premature beats of atrial and ventricular origin disturbing A-V rhythm in man are reported and compared with observations made by others in the experimental animal.

All premature beats were followed by noncompensatory pauses. In one instance evidence was obtained that the atrium was activated by the premature ventricular excitation.

In a case of upper A-V rhythm the restored beat after a premature ventricular contraction showed merging of the P wave and the QRS complex. An identical phenomenon was observed in the experimental animal and interpreted as due to temporary improvement in the conductivity of His's bundle secondary to retrograde transmission of the premature ventricular impulse to the A-V pacemaker.

Upright P waves in Leads II and III were observed in a case in which the sequence of ventricular and atrial contractions indicated the presence of lower A-V rhythm.

SUMMARIO IN INTERLINGUA

Pulsos prematur de origine atrial e ventricular que disturba le rhythmo atrio-ventricular in subjectos human es reportate e comparate con observationes facite per altere autores in experimentos animal.

Omne pulsos prematur esseva sequite per pausas noncompensatori. In un caso le datos observate supportava le conclusion que le atrio esseva activate per le prematur excitation ventricular.

In un caso de rhythmo atrio-ventricular superior le pulso restaurate post le prematur contraction ventricular exhibiva un fusion del unda P con le complexo QRS. Le mesme phenomeno esseva observate in experimentos animal ubi illo esseva interpretate como effecto de un melioration temporari in le conductivitate del fasce de His, secundari al transmission retrograde del prematur impulso ventricular al pacemaker atrio-ventricular.

Erecte undas P in derivationes II e III esseva observate in un caso in que le succession de contractiones ventricular e atrial indicava le presentia de rhythmo atrio-ventricular inferior.

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THE INFLUENCE OF CARBON DIOXIDE INHALATION ON ECTOPIC TACHYCARDIAS CAUSED BY VERATRINE

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WHEN veratrine is applied to the surface of the dog's ventricle, either by brushing or subepicardial injection, it elicits an ectopic tachycardia with rates which are slightly higher than those of the existing sinus rhythm. This ectopic tachycardia interferes with the sinus rhythm according to the rules governing parasystoles. Ventricular extrasystoles with fixed coupling are not observed.[19] Also, contrary to reports in the literature, ventricular extrasystoles with fixed coupling are not obtained when veratrine is administered intravenously.[18] Instead, only irregularly appearing ectopic beats are seen after the administration of a mixture of veratrine alkaloids, of veratridine, or cevadine. However, intraventricular and intra-auricular conduction disturbances and other arrhythmias are common, terminating in ventricular fibrillation.

This absence of fixed coupling of the ectopic beats was of interest because veratrine, more than any other substance, prolongs and intensifies the negative afterpotential and the supernormal phase. According to one widely accepted theory, the appearance of coupled extrasystoles seen shortly after the T wave (early in diastole) is due to the hyperexcitability of the heart caused by the supernormal phase.

In the present series of experiments the influence of carbon dioxide inhalation on arrhythmias produced by veratrine was studied. Previous experiments[17] have shown that ectopic impulse formation due to aconitine is markedly modified by carbon dioxide.

METHOD

The experiments were performed on twenty-six dogs. The dogs were anesthetized by the intraperitoneal administration of morphine (160 to 200 mg.) and Nembutal (3 to 4 ml.). The heart was exposed with vagi intact, after the institution of artificial respiration, as described in previous communications by the authors. The reason for using morphine and leaving the vagi intact was to permit a slower heart rate, thus allowing extrasystoles to appear.

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A mixture of veratrine alkaloids (Merck) was used. Five milligrams of the alkaloids were dissolved in 5 N hydrochloric acid and then neutralized with 5 N sodium hydroxide. This solution was made up to 10 ml. by the addition of distilled water. With a tuberculin syringe approximately 0.05 ml. of the solution was injected subepicardially in the outflow tract of the right ventricle, or in the lateral apical area of the left ventricle.

The carbon dioxide was supplied from cylinders as delivered by the manufacturer, containing a mixture of 20 per cent carbon dioxide and 80 per cent oxygen. The gas flowed into a basal metabolism tank (3 liters capacity) and then via electrically driven bellows into the dog's trachea. The inhalation of carbon dioxide was started immediately after the application of veratrine.

The electrocardiogram was registered in Lead II. In most experiments the recording was continued throughout the period of administration of the carbon dioxide and for two to four minutes following the cessation of it.

RESULTS

The concentration of carbon dioxide used for these experiments caused neither significant changes in the sinus beats of the electrocardiogram nor any significant dilatation of the heart.

Table I is a summary of the twenty-six experiments. After an initial ventricular tachycardia, produced by the application of veratrine, a bigeminal rhythm appeared during the breathing of the carbon dioxide-oxygen mixture in twenty-one of these experiments. In a few experiments a tachycardia and coupled extrasystoles were not observed, because the sinus rhythm was too fast to permit the ectopic beats to appear. In the experiment of June 8, 1954, during the inhalation of the carbon dioxide-oxygen mixture, a bigeminal rhythm appeared after four minutes without being preceded by an ectopic tachycardia. The inhalation of these gases did lead to a slowing of the sinus rhythm in most instances, thus allowing extrasystoles to appear. It has also been pointed out in our previous reports that the administration of too large a dose of barbiturate inhibits the formation of ectopic beats under the conditions of these experiments. This was apparently the reason why ectopic beats did not appear in some experiments.

The ectopic tachycardia appeared in twenty-one of the experiments within sixty seconds after the topical application of the drug. Usually the veratrine-induced tachycardias (elicited by topical application) disappear within one to two minutes, but under the influence of the carbon dioxide they were sometimes of longer duration, and in one experiment lasted for seven minutes. This prolongation of the ectopic rhythms by carbon dioxide-oxygen inhalation was also seen when sodium chloride, sodium citrate, or oxalate was used topically as the inducing agent.

The bigeminal or trigeminal rhythms (one or two extrasystoles following each normal beat) were occasionally continuous, but more often one or two normal sinus beats were interposed among the bigeminal and trigeminal groups (Figs. 1 to 3). The coupling was constant but with continued breathing of the carbon dioxide-oxygen mixture it shortened (Fig. 1). In some experiments the bigeminal

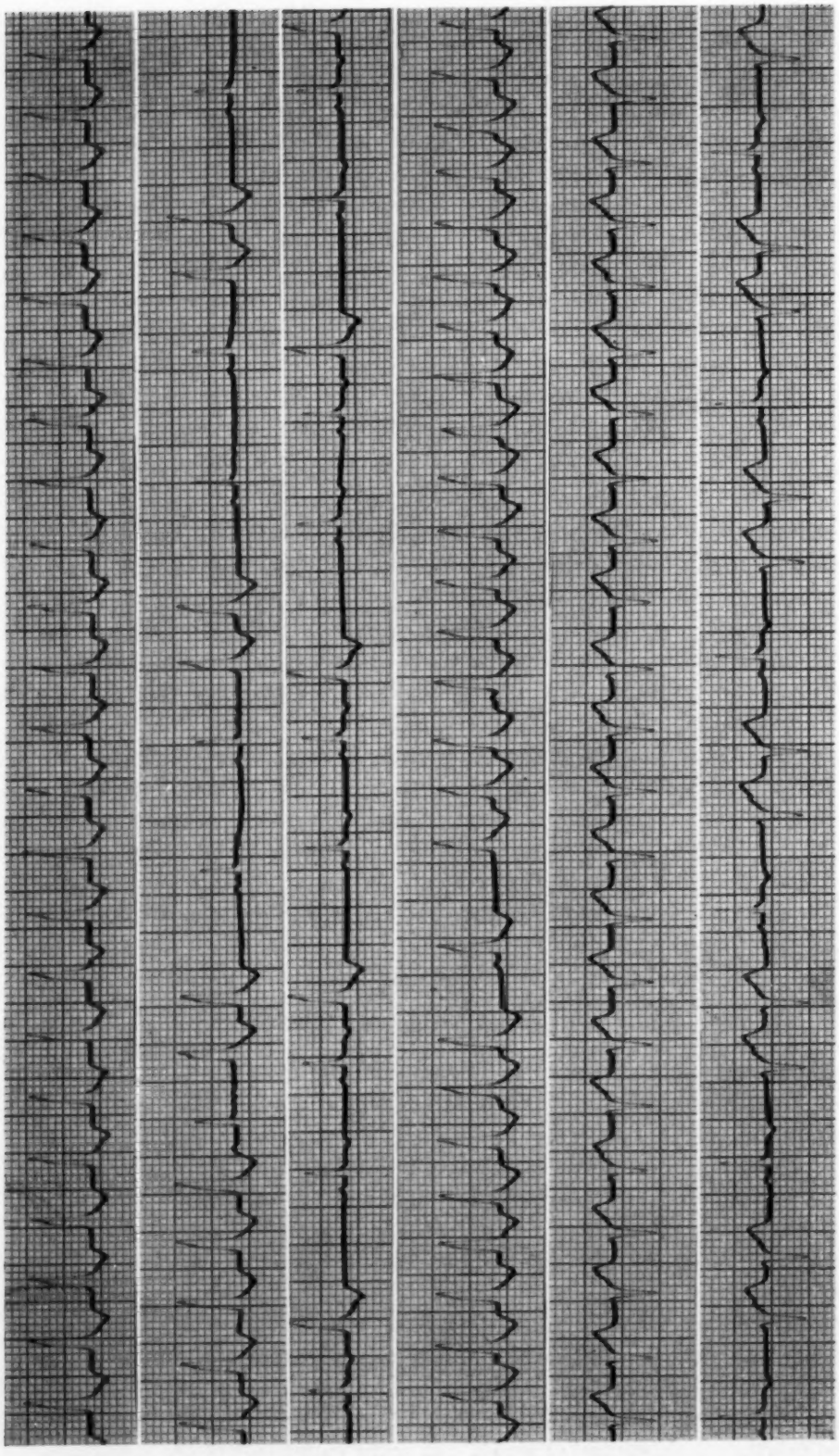

Fig. 1.—Experiment of May 18, 1954. The application of veratrine to the right ventricle causes a regular ventricular tachycardia with a rate of 144 per minute (*A*). The administration of the mixture of 20 per cent carbon dioxide and 80 per cent oxygen for 7 minutes, 10 seconds leads to the appearance of ventricular extrasystoles with fixed coupling. *B* reveals the transition from the regular tachycardia to trigeminal groups and soon (*C*) bigeminal groups appear separated by normal sinus beats without extrasystoles. The coupling during the trigeminal rhythm measures constantly 0.40 second and 0.32 second during the bigeminal rhythm. *D* demonstrates that rebreathing of atmospheric air for 1 minute, 50 seconds causes a reappearance of the tachycardia, this time with a rate of 214 per minute. Fourteen minutes later the application of veratrine to the left ventricle again elicits a ventricular tachycardia with a rate of 176 per minute (*E*). Inhalation of the carbon dioxide-oxygen mixture for 2 minutes, 10 seconds caused the appearance of a regular trigeminal rhythm with a coupling of 0.46 second (*F*). The extrasystoles during the tachycardia and the trigeminal rhythm have the same form.

regular trigeminal rhythm with a coupling of 0.46 second (*F*).

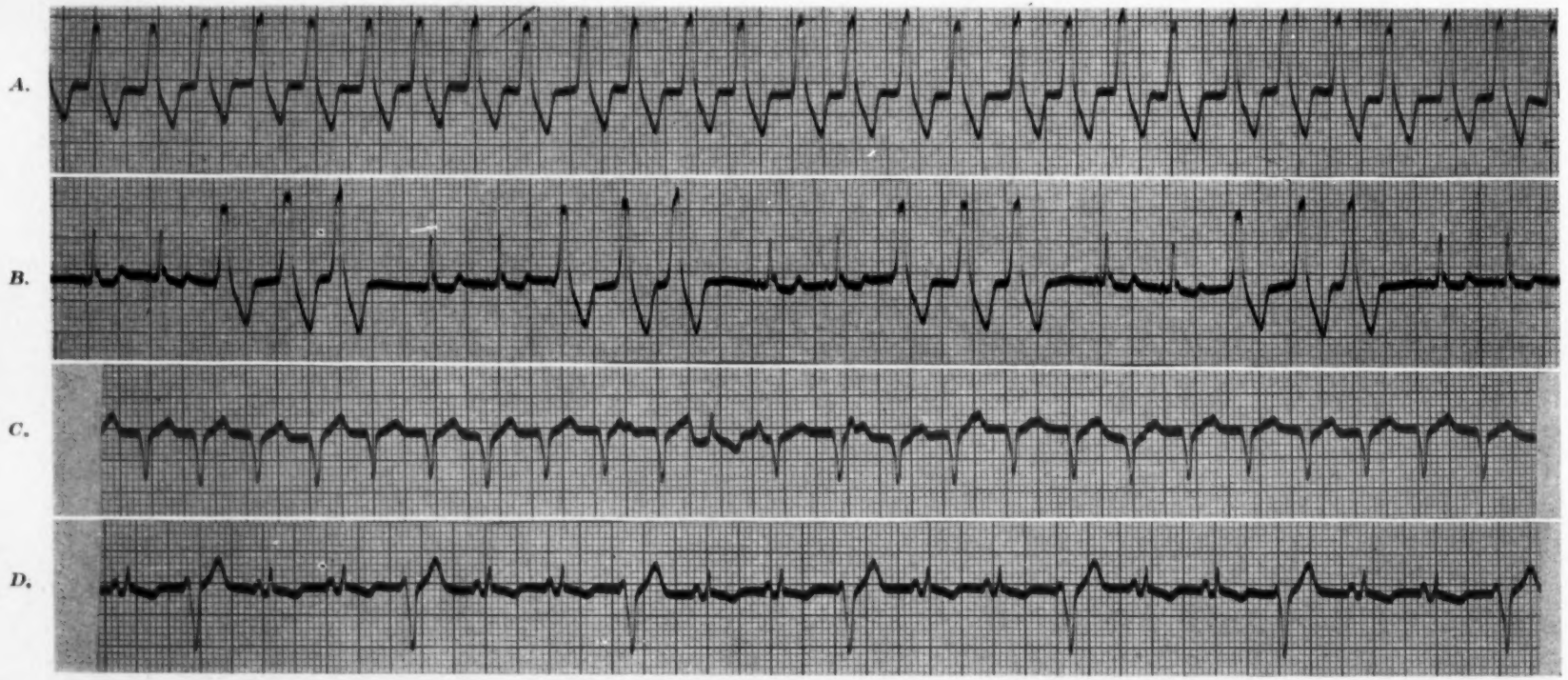

Fig. 2.—Upper two tracings, experiment of Feb. 8, 1955; lower two tracings, experiment of Feb. 1, 1955. *A* shows that after the application of veratrine to the right ventricle, a continuous ventricular tachycardia with a rate of 188 per minute appears. After the inhalation of the carbon dioxide-oxygen mixture for 7 minutes, 45 seconds, three extrasystoles follow every second normal beat. The coupling was constant at 0.36 second (*B*). In *C*, a left ventricular tachycardia (rate 166 per minute) resulted after the application of veratrine to the posterior apical area of the left ventricle. There is an interference with the sinus rhythm and one sinus beat is conducted to the ventricle. The mechanism is parasystolic. Following the inhalation of the carbon dioxide-oxygen mixture for eight minutes, every second sinus beat is followed by a left ventricular extrasystole with a coupling of 0.38 second.

TABLE I. SUMMARY OF THE RESULTS OF 26 EXPERIMENTS

DATES OF EXPERIMENTS	SITE OF APPLICATION OF VERATRINE	DURATION OF CO_2 INHALATION	RESULTS
12/29/53	Right ventricle	4 min. 20 sec.	Bigeminal rhythm
4/ 6/54	Right ventricle	2 min. 30 sec.	Bigeminal and trigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 2 min.
5/18/54	Right ventricle	7 min. 10 sec.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 1 min. 30 sec.
	Left ventricle	2 min. 10 sec.	Bigeminal rhythm
	Left ventricle	3 min. 20 sec.	Bigeminal rhythm
6/ 1/54	Left ventricle	3 min.	Bigeminal rhythm
6/ 8/54	Right ventricle	4 min.	Bigeminal rhythm, but not preceded by a tachycardia
6/22/54	Right ventricle		No veratrine-induced arrhythmia
6/29/54	Left ventricle	4 min. 30 sec.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 2 min. 10 sec.
10/ 5/54	Right ventricle		No veratrine-induced arrhythmia
10/12/54	Right ventricle	5 min. 30 sec.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 2 min.
10/19/54	Right ventricle		No veratrine-induced arrhythmia
10/26/54	Left ventricle	7 min.	Bigeminal rhythm
	Right ventricle	4 min. 5 sec.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 2 min. 10 sec.
11/ 9/54	Left ventricle	6 min.	Bigeminal rhythm
11/16/54	Left ventricle	3 min.	Bigeminal rhythm
11/23/54	Left ventricle	5 min.	Bigeminal rhythm
	Right ventricle	4 min.	Bigeminal rhythm
12/ 7/54	Left ventricle	4 min. 20 sec.	No effect
12/14/54	Right ventricle	6 min.	Bigeminal rhythm
	Left ventricle	2 min. 5 sec.	Bigeminal rhythm
12/21/54	Right ventricle	4 min.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 2 min. 40 sec.
12/28/54	Right ventricle	4 min. 20 sec.	Bigeminal rhythm
	Left ventricle	6 min.	Bigeminal rhythm
1/ 4/55	Left ventricle	3 min. 8 sec.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 2 min. 30 sec.
	Right ventricle	3 min.	Bigeminal rhythm; tachycardia returns after rebreathing atmospheric air for 3 min.
1/11/55	Left ventricle	7 min.	Bigeminal rhythm
	Right ventricle	9 min. 40 sec.	Bigeminal rhythm
1/18/55	Right ventricle	6 min. 50 sec.	No effect
2/ 1/55	Left ventricle	8 min.	Bigeminal and trigeminal rhythm (tachycardias only following vagus stimulation)
2/ 8/55	Right ventricle	7 min. 45 sec.	Bigeminal and quadrigeminal rhythms
3/15/55	Right ventricle	2 min. 30 sec.	Bigeminal rhythm
3/22/55	Left ventricle	4 min. 10 sec.	Bigeminal rhythm
4/26/55	Right ventricle	3 min.	Bigeminal rhythm
	Left ventricle	2 min. 30 sec.	Bigeminal rhythm

rhythm appeared suddenly, but more often single sinus beats appeared among the ectopic rhythms and the chains of ectopic beats progressively shortened until finally bigeminy was established. The earliest appearance of a bigeminal rhythm was after two minutes and ten seconds of carbon dioxide-oxygen mixture inhalation. In one experiment its appearance was delayed until nine minutes and forty seconds had elapsed. The average time for the reappearance of the tachycardia, after the rebreathing of atmospheric air, was two minutes. This was not observed in all experiments since the effect of veratrine is brief, and only in a few experiments lasted long enough to permit the tachycardia to reappear.

When the tachycardia reappeared after the rebreathing of atmospheric air, single ectopic beats were dropped in three experiments causing a pause of approximately double the length of a normal ectopic period (Fig. 4). This is caused by an exit block, and proves that a circus movement is not responsible for the tachycardia, for a circus wave cannot stop and start again spontaneously.

The bigeminy with constant coupling is certainly not caused by a parasystolic interference of two rhythms with approximately equal rates. This is evidenced by the long postextrasystolic pause following each extrasystole without any ectopic impulse formation (Figs. 1 to 3).

In four of the twenty-six experiments vagus stimulation by a faradic current caused the appearance of a paroxysmal auricular flutter or fibrillation which disappeared within a few seconds (Fig. 5). This phenomenon was observed immediately after the cessation of the administration of the carbon dioxide-oxygen mixture and while the dog rebreathed atmospheric air. The second effect of vagus stimulation, immediately after the rebreathing of atmospheric air, was the reappearance of groups of ectopic beats as seen in four experiments (Fig. 5). A third influence of vagus stimulation was the reappearance of an ectopic tachycardia. If the vagi were stimulated a few minutes after the discontinuation of the breathing of the carbon dioxide-oxygen mixture, ectopic beats appeared which continued with a rapid rate, even though vagus stimulation had been discontinued.

DISCUSSION

The influence of carbon dioxide on impulse formation in the heart has been studied rarely in spite of the fact that Gross found in 1903 that the mammalian heart exhibited cessation of impulse formation and nonresponse to mechanical and electrical stimuli after it had been perfused with Ringer's solution which had been saturated with carbon dioxide.[7]

When a method was found to elicit a regularly occurring bigeminal rhythm in the dog's heart in situ, by the cautious intravenous administration of aconitine, the influence of asphyxia on this arrhythmia was studied.[17] In fifteen of the nineteen experiments asphyxia caused the disappearance of the extrasystoles, while in the others a paroxysmal tachycardia appeared. When the animals were permitted to rebreathe atmospheric air, the bigeminal rhythm reappeared. Further analysis showed that the inhalation of a mixture of 3 per cent oxygen and 97 per cent nitrogen did not influence the arrhythmia, while the inhalation

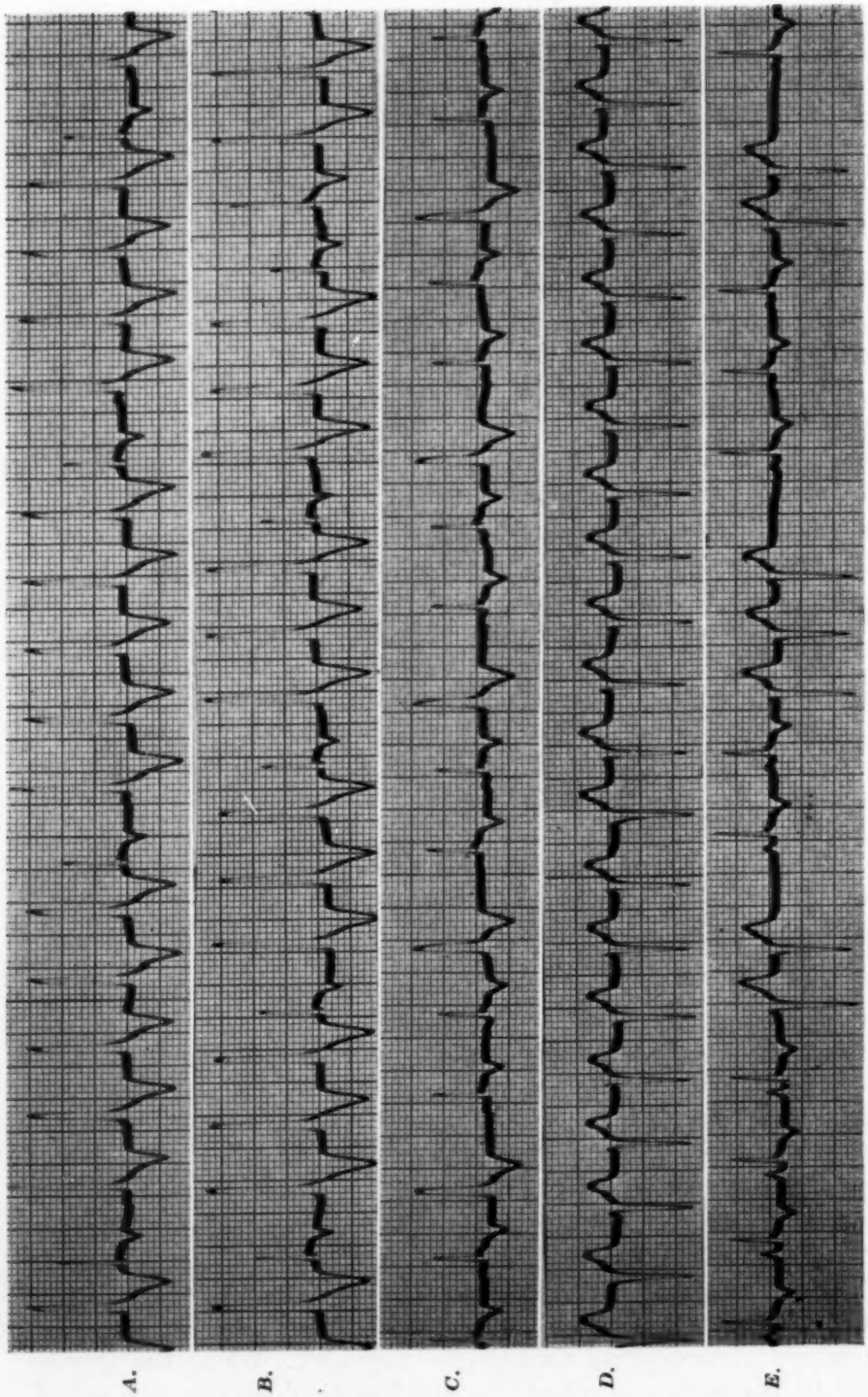

Fig. 3.—Experiment of Nov. 23, 1954. Veratrine applied to the outflow tract of the right ventricle had caused a regular ventricular tachycardia with a rate of 150 per minute. After four minutes of inhalation of the carbon dioxide-oxygen mixture sinus beats appear followed by four to five extrasystoles (*A*). Shortly afterwards regularly occurring three extrasystoles appeared after each sinus beat and then every second sinus beat was followed by one extrasystole. The coupling measures in *A*, 0.44 second, and in *B* and *C*, 0.40 second. In *D* the application of veratrine to the apical area of the left ventricle caused a ventricular tachycardia originating from this location with a rate of 142 per minute. After the inhalation of the carbon dioxide-oxygen mixture for five minutes, ventricular extrasystole appeared with fixed coupling (*E*). The coupling again measures 0.40 second.

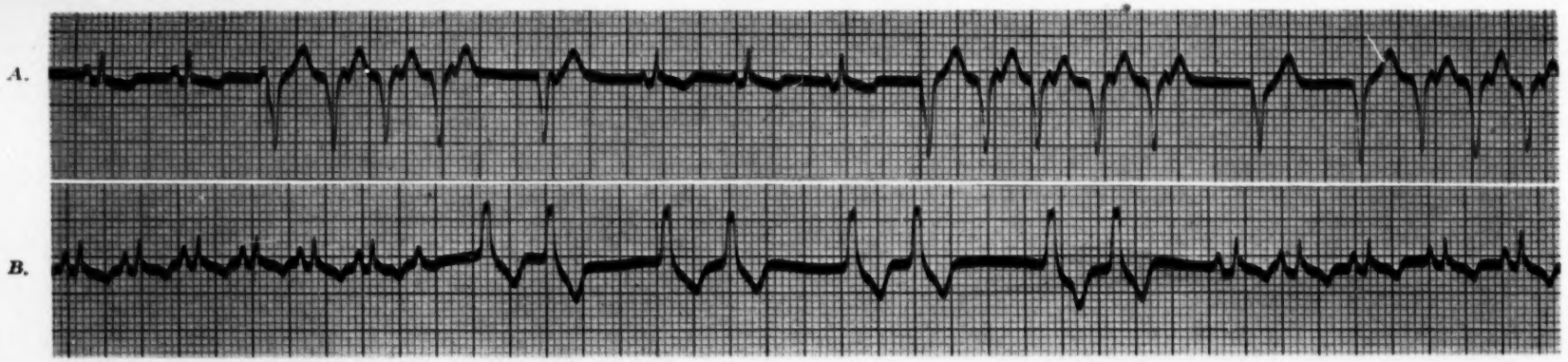

Fig. 4.—*A*, from the experiment of Feb. 1, 1955, shows an arrhythmia observed forty-five seconds after the discontinuation of an eight-minute period of administration of the carbon dioxide-oxygen mixture. The bigeminal rhythm caused by the carbon dioxide changes gradually into chains of extrasystoles, but on three occasions pauses are visible between the ectopic beats. The length of these pauses is equal to twice the interval between the ectopic beats. Therefore, an exit block from the ectopic center must be assumed. In *B*, the dog had received the carbon dioxide-oxygen mixture for five minutes after the focal application of a 10 per cent solution of sodium chloride to the ventricle. Vagus stimulation inhibits the sinus center and ectopic beats appear in groups.

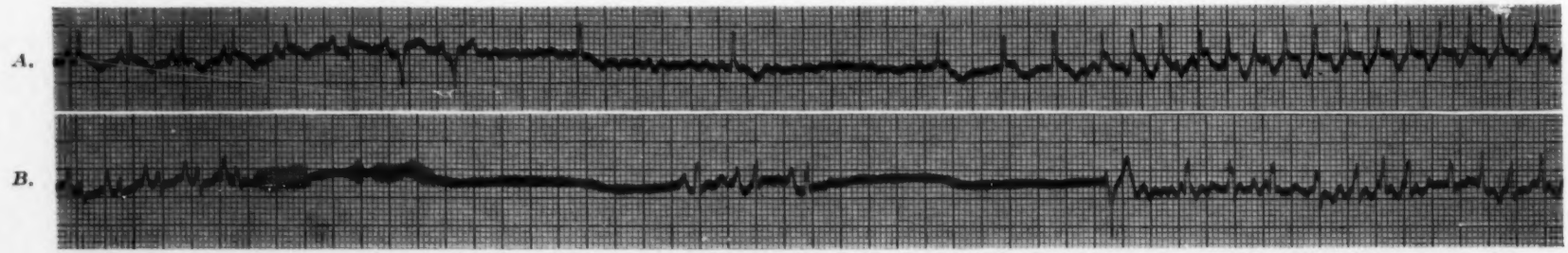

Fig. 5.—*A* is from the experiment of Dec. 7, 1954. Faradic stimulation of the vagus nerve one minute after the cessation of the administration of the carbon dioxide-oxygen mixture for seven minutes reveals the appearance of two ectopic beats. Then auricular fibrillation sets in immediately, which changes to flutter as soon as the vagus stimulation is interrupted. The flutter disappeared twenty-seven seconds later. *B* was obtained from an experiment of Jan. 11, 1955. Vagus stimulation after the end of an eight-minute period of carbon dioxide inhalation causes a long inhibition of the sinus node, and, suddenly, auricular fibrillation sets in. It disappeared twenty seconds later.

of a mixture of 20 per cent carbon dioxide and 80 per cent oxygen elicited the same effects as the asphyxia. From this the conclusion was drawn that, among other factors, during asphyxia it is mainly the accumulation of carbon dioxide which abolishes the extrasystoles.

After the intravenous injection of strophanthin, inhalation of carbon dioxide causes the appearance of a bigeminal rhythm.[6] In the normal animal this is not observed if just digitalis or strophanthin is injected. Later, in the same laboratory, the influence of carbon dioxide on barium-induced extrasystoles was studied in dogs.[4] The afore-mentioned results were confirmed. The irregular tachycardia which typically appears under the influence of these compounds disappeared and was changed into a polygeminal and bigeminal rhythm; finally sinus rhythm appeared. When the animal was permitted to rebreathe atmospheric air the ectopic rhythm which was initially observed reappeared.

Thus the available results show that the inhalation of a mixture of carbon dioxide and oxygen abolishes the bigeminal rhythm caused by aconitine and the irregular tachycardias due to strophanthin or barium chloride, when the latter are given intravenously.

This gas mixture prolongs, in the experiments reported in the present paper, ectopic tachycardias caused by sodium oxalate, sodium citrate, or sodium chloride applied topically to the dog's heart. It initially prolongs the tachycardias caused by topically applied veratrine and finally transforms them into a bigeminal rhythm. When veratrine is given topically or systemically, bigeminal rhythm is not observed without the use of carbon dioxide.

With the recognition in recent years of the importance of potassium for the appearance of certain arrhythmias under specific conditions, for instance during the administration of digitalis, the finding is important that narcotic concentrations of carbon dioxide in the cat causes a rapid rise of plasma potassium. A concentration of 34 per cent carbon dioxide causes a rise of the plasma potassium, reaching a peak in five and one-half minutes and gradually returning to normal when the administration of carbon dioxide is discontinued.[13] On removal of the carbon dioxide a secondary smaller rise of potassium is observed. The plasma concentration of potassium rises in acidosis; it seems to move from the cells into the extracellular fluids.[1,9]

In this connection the observation is important that after prolonged inhalation of high concentrations of carbon dioxide (30 to 70 per cent) by dogs, the sudden cessation of the administration of carbon dioxide (thus reducing the alveolar concentration to normal) causes ventricular fibrillation to occur.[2,16] Arrhythmias begin within thirty seconds to six minutes after the rapid fall of the high carbon dioxide tension in the alveoli. Significant is the appearance of marked intraventricular conduction disturbances before the onset of these arrhythmias, for intraventricular conduction disturbances and block are a typical consequence of hyperpotassemia.

Young found a progressive rise in plasma potassium in dogs during the inhalation of a 30 to 45 per cent concentration of carbon dioxide.[21] In keeping with the results mentioned above, immediately after stopping the administration of carbon dioxide, there was a sharp secondary rise in the plasma potassium.

It was at this point that the arrhythmias appeared.

After a short exposure to carbon dioxide (up to 10 minutes), such as we used in our experiments, a similar phenomenon was not observed.

Of great importance for the understanding of the effect of carbon dioxide on impulse formation are studies by neurophysiologists, particularly Lorente de Nò.[11] Under various conditions carbon dioxide, in the concentration of 5 per cent, was found to inhibit the firing of impulses in the mammalian and frog nerve. It increases the membrane potential (the L fraction), raises the threshold for stimuli, prolongs the duration of afterpotentials,[3] counteracts depolarizing agents like veratrine, barium, or potassium, and causes reduction or cessation of rhythmic firing of impulses in a nerve treated with sodium citrate, sodium oxalate, or barium chloride.[15]

Carbon dioxide abolishes the afterdischarge seen if a nerve treated with barium chloride is electrically stimulated.[12] The depolarizing action of veratrine is counteracted by carbon dioxide which tends to restore the membrane potential to its normal level. These actions of carbon dioxide are specific and are not due to a lowering of the pH. All these factors diminish or inhibit firing of impulses. On the other hand, the prolongation and enhancement of the negative afterpotential (supernormal phase) may explain the prolongation of the ectopic tachycardias observed by us under the influence of carbon dioxide. These results show again the close parallelism between the response of hearts and nerve fibers to certain agents.

The fact that in asphyxia it is the accumulation of carbon dioxide which is the responsible agent for the disappearance of the extrasystoles and not the lack of oxygen[17] is important in view of the experimental work of Mathison concerned with the effect of asphyxia on A-V conduction in the cat. No conduction disturbance was seen even with a concentration of carbon dioxide up to 67 per cent. On the contrary, heart block caused by asphyxia disappeared when such high concentrations of carbon dioxide were inhaled, but quickly reappeared when a mixture of 2 per cent oxygen and 98 per cent nitrogen was used. If those who still assume that extrasystoles are caused by a type of circus movement and re-entry were right, then, in accordance with the results of Mathison, inhalation of nitrogen and not of carbon dioxide should abolish the extrasystoles. The slowing of the conduction in nerves by carbon dioxide has been confirmed.[3]

The appearance of auricular flutter or fibrillation during stimulation of the vagus nerve is known to occur. It is an occasional phenomenon observed in animal experiments but is rarely seen in man. The observation that it occurred four times immediately after the administration of carbon dioxide was discontinued in our experiments is hardly fortuitous. An explanation is difficult but it is possible that changes in the electrolyte content of the myocardium are responsible. An enhancement of the effect of vagal stimulation on the heart, caused by breathing of 20 per cent carbon dioxide, has been described.[20,22] It has been claimed, that under the influence of carbon dioxide, acetylcholine is more slowly destroyed[5] so that it reaches higher concentrations and exerts a greater inhibitory action. Hypercapnia was found to increase the peripheral excitability of the vagus nerve endings.[8]

SUMMARY

Veratrine alkaloids, applied topically on the dog's ventricle or given intravenously, do not elicit extrasystoles with constant coupling. Such extrasystoles appeared, however, in twenty-one out of twenty-six experiments, when veratrine was applied topically to the ventricular surface of the dog's heart and the animal inhaled a mixture of 20 per cent carbon dioxide with 80 per cent oxygen. Before the appearance of the extrasystoles with fixed coupling a prolongation of the ectopic tachycardia, which typically follows application of veratrine, could be observed. In a similar way ectopic rhythms following topical application of sodium chloride, sodium citrate, and sodium oxalate were prolonged; bigeminal rhythms were common.

Following the inhalation of carbon dioxide the phenomenon of exit block was seen in a few experiments and vagal stimulation elicited ectopic auricular and ventricular rhythms.

An attempt is made to explain the described action of carbon dioxide on the basis of known neurophysiologic data.

SUMMARIO IN INTERLINGUA

Alcaloides veratrinic, applicate topicamente al ventriculo canin o administrate intravenosemente, non evoca extrasystoles a copulage fixe. Nonobstante, in 21 ex 26 experimentos tal extrasystoles a copulage fixe se manifestava post le application topic de veratrina al superficie ventricular del corde canin si le animal inhalava un mixtura de 20 pro cento dioxydo de carbon con 80 pro cento oxygeno. Ante le apparition del extrasystoles a copulage fixe nos observava un prolongation del tachycardia ectopic que es un typic sequentia del application de veratrina. Un simile prolongation occurreva in le rhythmos ectopic que seque le application topic de chlorido de natrium, citrato de natrium, e oxalato de natrium. Rhythmos bigemine esseva commun.

Post le inhalation de dioxydo de carbon le phenomeno del bloco de exito esseva observate in un numero de experimentos, e stimulation vagal evocava ectopic rhythmos auricular e ventricular.

Nos essaya explicar le supra-describite effecto de dioxydo de carbon super le base de cognoscite datos neurophysiologic.

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EISENMENGER'S COMPLEX. A CLINICAL AND PATHOLOGIC STUDY OF FOUR CASES

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MEXICO, D. F.

TO THE typical cases of the so-called tetralogy of Eisenmenger, several kinds of atypical cases could be added. These are usually difficult to diagnose, and they include those cases resembling a patent ductus arteriosus in view of an added and possibly acquired aortic insufficiency; they also include cases with an aorta which is not only dextroposed, but completely originating from the right ventricle.

There is, finally, a peculiar form of Eisenmenger's complex where a spontaneous correction of one of the elements of the tetralogy, namely the closure of the interventricular septal defect by the septal leaflet of the tricuspid valve has taken place.

The purpose of this paper is to discuss at least one example of each of these bizarre forms of the Eisenmenger complex.

Eisenmenger's report[1] was antedated by others, but his paper has remained a classic. Yet, it was Abbott[2] who contributed to a clear understanding of this malformation, by pointing out the importance of a biventricular origin of the aorta.

Our former experience at the National Institute of Cardiology has consisted of two clinical cases, one of which was proved with catheterization studies.[3] Of a total of nearly 1,500 cases of congenital heart disease, our six cases constitute a small portion: less than three out of every thousand congenital hearts.

Embryology.—In this malformation there is an equal partition of the primitive trunk; if it is unequal, the pulmonary artery remains the larger vessel. The aorta remains somewhat small, and it overrides the ventricular septum in varying proportions, ranging from a minimal overriding to a complete dextroposition, in which case the aorta springs entirely from the right ventricle.[4] Occasionally the aorta is not only small but hypoplastic.[5]

Some authors[6] insist on the structural changes observed in the pulmonary vessels as an integral part of the malformation. Others maintain that these changes are due to the hemodynamics of this type of heart.[7-11] It is evident, in any case, that these changes are observed in the Eisenmenger heart, and it appears quite evident, also, that the pulmonary circuit is subject to high pressure, of the systemic type, in view of the presence of the interventricular septal defect and the biventricular origin of the aorta.

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One of us[12] has previously emphasized the difficulty of a correct clinical diagnosis during life, particularly the differential diagnosis with a ventricular septal defect.[13] In both cases the dynamic behavior as judged under the fluoroscope is quite similar, and it is possible that some of the simple interventricular septal defects closely resemble an Eisenmenger complex. It is the biventricular origin of the aorta that is difficult to diagnose, not only clinically but sometimes even at autopsy.[14]

On the other hand, the clinical picture of cases with this malformation has been atypical quite often, leading the clinician to erroneous diagnoses and, at times, to useless operations. Hurst and Schemm's,[15] Taussig and Semans',[16] and two of the cases of our series are examples of this unusual picture which made the diagnosis impossible.

Fig. 1.—Portable x-ray. The heart is moderately enlarged. The pulmonary segment is straight. The aortic knob seems to arch to the right. There is a marked hilar congestion.

CASE REPORTS

CASE 1.—The patient was a 20-year-old man who had always been well. One month before he died he suddenly experienced a sharp precordial pain; cough and hemoptysis followed, after which dyspnea and heart failure ensued. On physical examination there was a precordial bulging, the apical impulse was felt at the sixth left intercostal space, about 12 cm. from the midline. A systolic and diastolic thrill were clearly felt over the second left intercostal space; a systolic and diastolic murmur were clearly audible at the pulmonary area. Blood pressure was 130/0 mm. Hg. The pulse was Corrigan in type. The patient was never cyanotic and had no clubbing. Laboratory examinations revealed 5.2 million red cells; 96 per cent hemoglobin and 13,000 white blood cells. The electrocardiogram was suggestive of left ventricular hypertrophy and digitalis action. X-ray showed an enlarged heart with a slightly prominent pulmonary segment and increased vascular markings (Fig. 1).

The patient was in poor condition at the time of admission, and all therapeutic measures failed. He soon died. The diagnosis was congenital heart disease, patent ductus arteriosus, and congestive heart failure.

Autopsy.—(Study limited to the heart.) The heart was enlarged; both ventricles were hypertrophied. Both venae cavae entered normally into the right auricle, which was slightly dilated. The tricuspid valve was normal. The right ventricle was dilated and hypertrophied; its wall measured 11 mm. in thickness at the outflow chamber. The pulmonary artery was normally

Fig. 2.

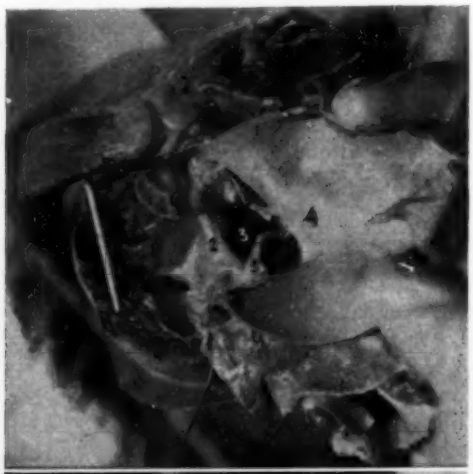

Fig. 3.

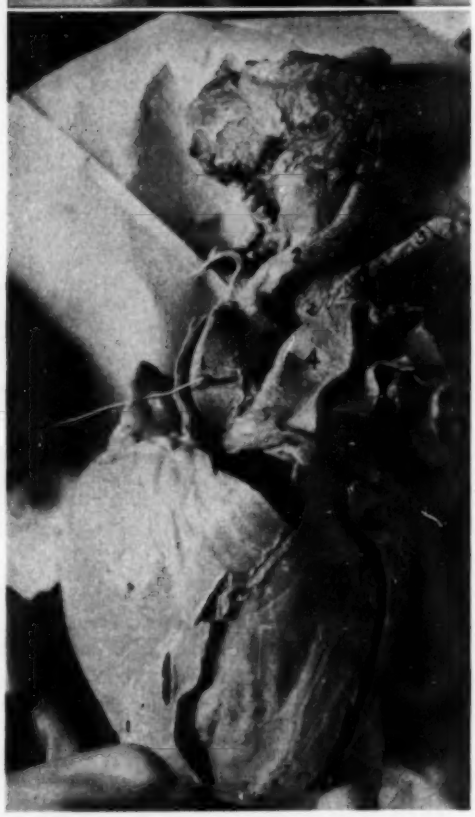

Fig. 2.—The heart of Case 1 seen from above. *1* marks the cavity of the right ventricle; *2*, the upper portion of the interventricular septum at the level of the septal defect; *3*, the left ventricular cavity; *4*, the ascending aorta; *5*, the two normal aortic cusps; *6*, the overriding cusp, which is larger than the other two, fenestrated and deformed; it bulges into the right ventricle.

Fig. 3.—The heart and great vessels of Case 1. *1* is the aortic arch, crossing to the right of the trachea; *2* is the first branch given off by the aorta, the left carotid; *3* is the aberrant left subclavian, given off by the descending aorta and crossing behind the esophagus; *4* is the dilated pulmonary trunk.

situated and showed no abnormalities; it measured 65 mm. in circumference. The left auricle and the mitral valve were normal. The left ventricle was dilated and hypertrophied; its wall measured 17 mm. in thickness at the inflow chamber and 15 at the outflow chamber. The aorta was normal but it overrode the ventricular septum slightly, so that one-fourth of the vessel arose from the right ventricle (Fig. 2). There was a high ventricular septal defect which measured 23 mm. longitudinally. The supraventricular ridge measured 5 mm. in thickness. The aortic cusp overriding the septum was as large as the other two together. It was fenestrated and was,

Fig. 4.

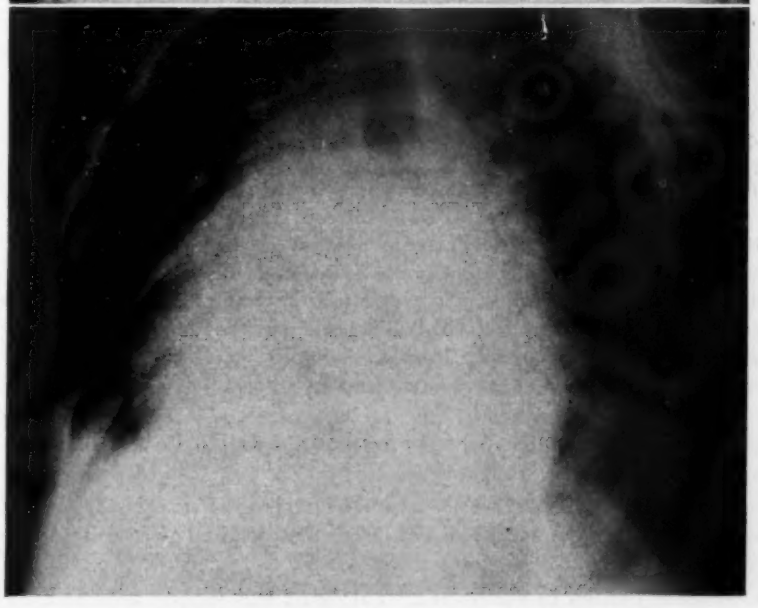

Fig. 5.

Fig. 4.—X-ray of Case 2, showing a moderate enlargement of the heart and a straight pulmonary segment. The aortic knob seems to arch to the right. There is a marked lung congestion.

Fig. 5.—The same case of Fig. 4 in the left oblique view. It shows biventricular hypertrophy.

in all probability, insufficient. The aorta measured 65 mm. in circumference, 4 mm. above the semilunar cusps. The vessel arched to the right and crossed the right aspect of the trachea (Fig. 3). It gave off the following branches: a left carotid, a right carotid, and a right subclavian, independently. The descending portion of the aorta gave off the left subclavian artery. This

branch crossed the posterior aspect of the esophagus, making a deep groove in it. This artery showed a fibrous cord corresponding to the obliterated ductus arteriosus. An incomplete vascular ring was formed around the trachea and the esophagus, which was formed by the right aortic arch, the left subclavian, the fibrous cord, and the pulmonary trunk.

CASE 2.—In a 7-year-old boy known to have dyspnea on effort and palpitations for the last four years prior to his death, a bronchial episode preceded the appearance of a rapidly progressive heart failure. When admitted to the Institute the patient was dyspneic and showed slight cyanosis but no clubbing. He was in congestive heart failure. The apex beat was felt at the fifth left intercostal space at the level of the midclavicular line. A harsh systolic thrill was felt over the entire precordium. A rough systolic murmur was well heard all over the precordial area, maximal at the fourth left intercostal space. It could be heard at the left axilla but it was

Fig. 6.—The heart seen from the apex into the right ventricle. *1* shows the aortic origin, behind the crista supraventricularis; *2*, the crista supraventricularis, measuring 15 mm. in thickness; *3*, the origin of the pulmonary artery; *4*, a huge papillary muscle. Right ventricular hypertrophy is evident.

not transmitted to the neck vessels. A gallop rhythm was present. The second pulmonary sound was accentuated. Numerous râles were heard at the lung bases. Edema was present in the legs and the abdominal wall. The liver was greatly enlarged. Blood pressure 100/90 mm. Hg. Laboratory examinations: Red cells and hemoglobin were normal. X-ray (Fig. 4) showed a moderately enlarged heart. The aorta seemed to arch to the right; the pulmonary segment was straight. Lung vascular markings were accentuated. In the left oblique (Fig. 5) a moderate enlargement of both ventricles was thought to be present. The electrocardiogram was suggestive of right auricular and ventricular hypertrophy, a right bundle branch block, and a doubtful left auricular enlargement.

The patient was thought to have a congenital heart lesion and possibly a rheumatic carditis. He was in poor condition when admitted and did not respond to digitalis and other supportive measures.

Autopsy.—(Study limited to the heart). The heart was slightly enlarged. The right ventricle was dilated and hypertrophied. Its inflow chamber wall measured 10 mm. in thickness. The thickness of the wall at the outflow chamber was 13 mm. The pulmonary artery was ample, measuring 50 mm. in circumference. It was slightly atheromatous. The valves were normal. The right and left auricles were normal and no communication was seen between them. The left ventricle was hypertrophied. Its wall measured 10 mm. in thickness at the inflow tract and 13 at the outflow tract. An oval-shaped ventricular septal defect was present, measuring 7 mm. in its greater diameter. The origin of the aorta could not be seen from the left ventricle above

this orifice. The supraventricular ridge measured 15 mm. in thickness. The aorta arose behind this structure and entirely from the right ventricle. It measured 15 mm. in diameter. An unusually large papillary muscle was present in the right ventricle, located under and slightly anterior to the supraventricular ridge. It united the septum with the free wall of the right ventricle, bridging between these two portions of the right ventricle. This structure, together with the supraventricular ridge, formed an incomplete division between the inflow and the outflow tracts of the right ventricle, the aorta arising from the inflow tract and the pulmonary from the outflow tract (Fig. 6). A slight degree of aortic coarctation was present. The coronary arteries were normal and the ductus was closed.

CASE 3.—A 16-year-old boy had a history of joint pains three months before he died. At this time he developed a cough and hemoptysis, and a temperature rise was recorded. Following these symptoms heart failure set in. On physical examination it was found that the right jugular vein was hard and painful. The precordial area was prominent. A rough and loud systolic murmur was heard in the midprecordial area. The second pulmonic sound was accentuated.

Fig. 7.—X-ray of Case 3. There is moderate heart enlargement. A triangular shadow is visible in the right chest, suggestive of a pulmonary infarct. There is also a pleural effusion.

A slight pericardial rub was audible. Laboratory examinations revealed 3.8 million red cells; hemoglobin 63.1 per cent and 15,600 white cells. The x-ray (Fig. 7) showed a cardiac shadow partially masked by a right pleural effusion. A triangular shadow was present in the upper portion of the right lung field, suggestive of a pulmonary infarct. The electrocardiogram suggested biventricular hypertrophy and a first degree A-V block. Despite digitalis therapy and other supportive measures the patient succumbed soon after admission. The patient was thought to have a congenital heart of the ventricular septal defect type, with an added rheumatic carditis and thrombophlebitis of the right jugular vein.

Autopsy.—(Study limited to the heart). The heart was moderately enlarged. The right auricle and ventricle were enlarged. There was no communication between the auricles. The tricuspid orifice measured 120 mm. in circumference. Its septal leaflet was not free. It was firmly attached to the septum by minute short cordae tendinae, but it projected into the right ventricular cavity (Fig. 8). The average thickness of the right ventricular wall was 3 mm.; at the level of the infundibulum it was 8 mm. The left ventricular wall was 14 mm. in thickness. The pulmonary artery was normal. The aorta was shaped like an hour glass, due to a marked narrowing located about 12 mm. above the semilunar cusps (Fig. 9), at which place it measured 25 mm. in circumference, and above it 42 mm. The aortic cusps were deep and narrow, exhibiting large fenestrations. Numerous fibrinous verrucae were seen at the narrow portion of the vessel. Finally, the aorta was dextroposed and was "overriding" the ventricular septum. Indeed, the membranous portion of the ventricular septum was lacking and an interventricular

septal defect was present. However, this defect was completely sealed by the septal leaflet of the tricuspid valve (Fig. 8).

CASE 4.—This case serves only to demonstrate the anatomy of a heart quite similar to the previous because it had a dextroposed aorta and an interventricular septal defect. This defect was partially occluded by the septal leaflet of the tricuspid valve, so that a probe could easily be passed from the right to the left ventricle (Figs. 10 and 11). No clinical or radiological studies were available in this case.

Fig. 8.

Fig. 9.

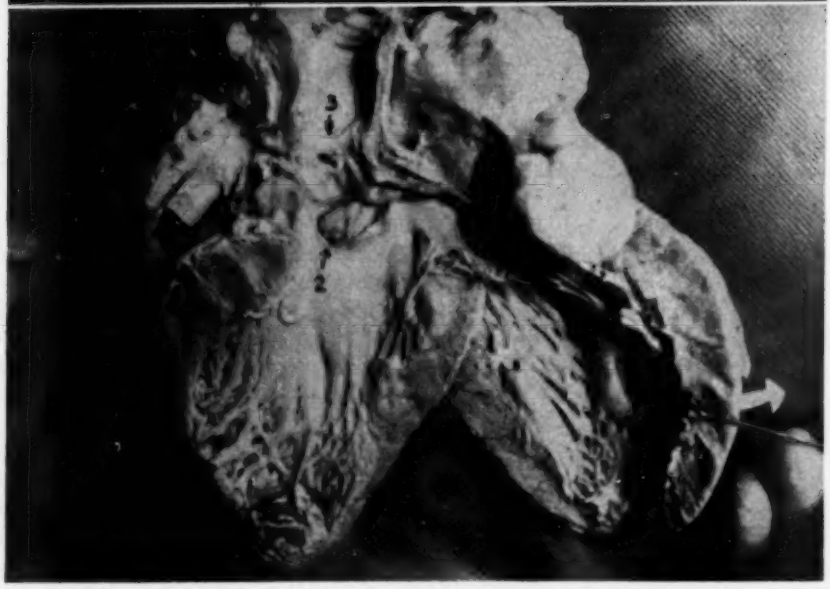

Fig. 8.—The heart of Case 3 seen from the right cavities. *1* points to the septal leaflet of the tricuspid valve. Notice that its "free" border is inserted by means of fine chordae tendinae to the septum; it protrudes into the right ventricular cavity. Compare it with the leaflet marked *2*.

Fig. 9.—The same case as Fig. 8 seen from the left ventricle. *1* indicates the septal leaflet of the tricuspid which obliterates the septal defect. The arrow, *2*, is pointing to the lower border of the interventricular defect, which is the highest portion of the muscular septum. *3* is the site of aortic narrowing. Notice that the aorta occupies a posterior plane with respect to the septum in this view; in other words, it is dextroposed and it "overrides" the septum. Left ventricular hypertrophy is evident.

DISCUSSION

Case 1.—The clinical data, namely the presence of a thrill and a systolic murmur, together with the bounding pulse and a blood pressure of 130/0 mm. Hg., led to the erroneous diagnosis of a congenital anomaly of the patent ductus arteriosus type. The complication which took place toward the end and precipitated the onset of heart failure is not remarkable, except perhaps that it was rapidly progressive. It is of interest that the immediate cause for this failure

Fig. 10.

Fig. 11.

Fig. 10.—The heart of Case 4 seen from the right cavities. The internal or septal leaflet of the tricuspid (*1*) is partially inserted by fine chordae tendinae to the wall of the ventricular septum. Between this leaflet and the septal defect (partially occluded by the leaflet), a probe may be passed. The leaflet marked *2* is normal.

Fig. 11.—The same case as Fig. 10. *1* shows one portion of the internal leaflet of the tricuspid valve incompletely occluding the septal defect, marked *2*. A probe is passed through the small orifice left by the abnormal leaflet. *3* shows the aorta, which, as in Case 3, "overrides" the ventricular septum and it is dextroposed.

was the appearance of a pulmonary infarct. In retrospect, it is unusual for this patient to have reached the age of 20 years, leading a perfectly active life until the moment he had the pulmonary infarct, which took place scarcely one month before his death. That this pulmonary complication is to be accounted for by a state of chronic lung congestion and less likely by congestion due to heart failure was evident at x-ray and it has been proved in lung sections (Fig. 12). It is reasonable to assume that this lung congestion with, or as a result of, pulmonary hypertension was possible in view of the presence of a biventricular aorta. Indeed, it is this anatomic feature which imposes a burden on the right ventricle by forcing it to face—at least partially—systemic vascular resistances.[8-10,17]

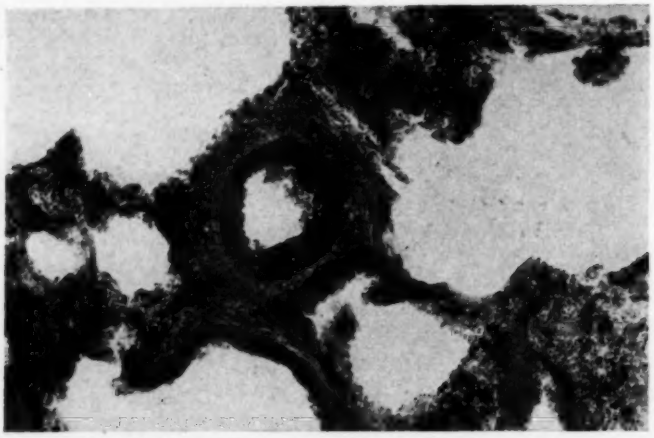

Fig. 12.—A lung section of Case 1. The small vessel is an arteriole showing slight thickening of the intima and some degree of hypertrophy of the media.

It has seemed to us that this case might have been suspected of being something other than a patent ductus, had it been known that a right aortic arch was present. Unfortunately, the only x-ray done was a portable, in view of the poor condition of the patient. But even this plate is suggestive of the right aortic arch (see Fig. 1). We decided to demonstrate the radiological appearance of this feature, by filling the esophagus with opaque substance. An x-ray proved this to be the case (Fig. 13). A lateral x-ray demonstrated another interesting feature: the presence of a deep retroesophageal notch, produced by the left subclavian as it passed behind the esophagus (Fig. 14). Again, these two radiological features might have aided in the diagnosis, as it seems to us that a right aortic arch is very often indicative of the coexistence of a bulboseptal malformation. In our experience with hundreds of cases of patent ductus arteriosus, the aortic arch has never been found to the right. On the other hand, this added anomaly is often found in tetralogy of Fallot, transposition of the great vessels, truncus arteriosus, and Eisenmenger's complex.

Case 2.—Although several features are consistent with the diagnosis of interventricular septal defect, the true diagnosis was not established, among other reasons because of the rarity of the malformation. In retrospect in this case too, it is worthwhile to mention the history of numerous bronchial episodes and especially the fact that one of these episodes was the immediate cause for the appearance of congestive heart failure. Despite the presence of minimal cyanosis, this symptom can be only taken as a terminal occurrence, since neither

polycythemia nor clubbing were present during life. It is remarkable that cyanosis was not more apparent in the presence of the right ventricular origin of the aorta.

Following Saphir and Lev's[4] and other author's views,[9] we admit this to be a case of Eisenmenger's complex with complete dextroposition of the aorta. All of the features belonging to this complex are present, including the microscopic findings pertaining to the vascular changes attributable to pulmonary hypertension (Figs. 15 and 16). Yet, it is well to emphasize the fact that in our case, the aorta and the pulmonary artery maintain a normal relationship, whereas

Fig. 13.

Fig. 14.

Fig. 13.—Postmortem x-ray of the heart of Case 1. The esophagus has been filled with barium; it is slightly pushed to the left by a right aortic arch.

Fig. 14.—X-ray of the same case as Fig. 13. Lateral view of the specimen. The barium-filled esophagus shows a marked forward displaced notch produced by a retroesophageal vessel: the aberrant left subclavian artery.

Saphir and Lev's case, in our estimation, is a true transposition of the great vessels because their mutual relation is altered.

Case 3.—Perhaps only the rough systolic murmur at the midprecordial area was suggestive of the presence of an interventricular septal defect. This patient also died in heart failure following a pulmonary congestion which can only be accounted for by the heart failure. Indeed, the aorta is unquestionably dextro-

Fig. 15.

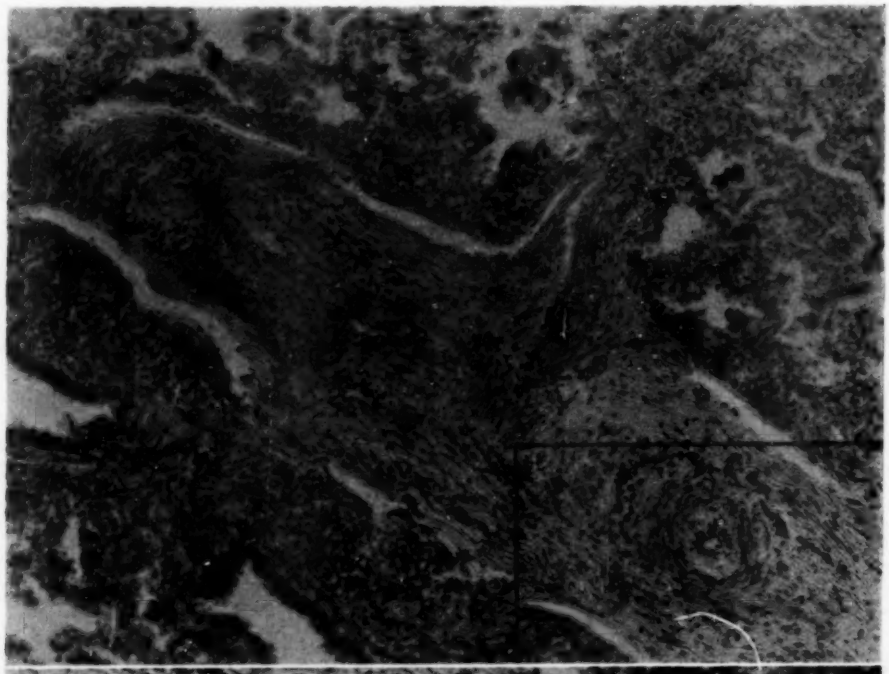

Fig. 16.

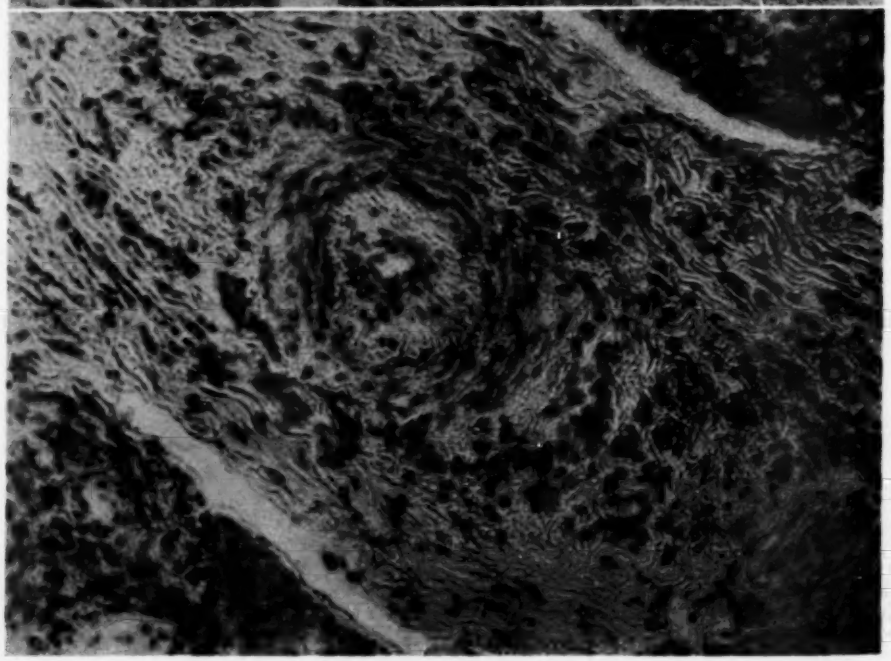

Fig. 15.—Lung section of Case 2 which shows some small arterioles with marked intimal thickening and medial hypertrophy.

Fig. 16.—An enlargement of the right lower angle of Fig. 15. Compare this figure with Figs. 12 and 17.

posed but it is not biventricular because of the occlusion of the interventricular septal defect by the septal tricuspid leaflet: hence, it does not influence the dynamics of the right ventricle. This view receives support in the pathologic study of lung sections which leads to the conclusion that there are no vascular changes (Fig. 17). It follows that no hypertension of significant degree was present and that cyanosis—when it appears—in Eisenmenger's complex, must be due to vascular changes produced by the altered hemodynamics as a consequence, in turn, of a biventricular aorta. Therefore vascular abnormalities are not a congenital feature in Eisenmenger's complex.[18] It is probable that heart failure in this case was in great part due to the presence of the aortic stenosis described. There is no clinical evidence that tricuspid regurgitation was present during life. Heart failure in any case was a terminal and rapidly progressive condition.

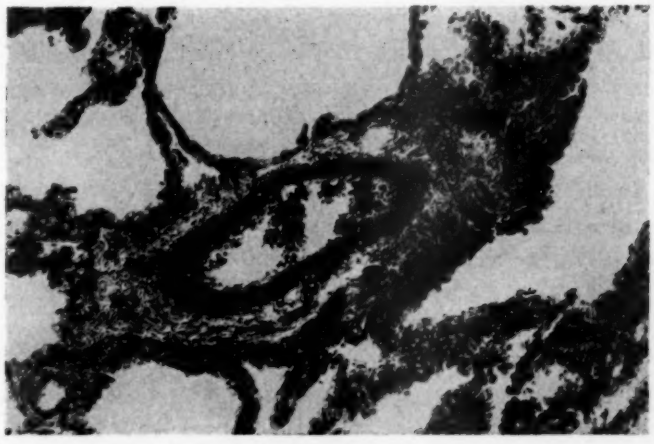

Fig. 17.—Lung section of the case of "corrected" Eisenmenger. This small arteriole is completely normal.

CONCLUSIONS

1. This study includes four cases of Eisenmenger's complex with autopsy reports. Two of the cases are peculiar in that they exhibit a spontaneous correction of the interventricular septal defect by the total or partial attachment of the septal leaflet of the tricuspid valve to the septum.[19-22]

2. Aortic dextroposition is evident in all cases. In the first it was slight and in the second it was totally dextroposed. This maximal degree of dextroposition is compatible with the diagnosis of Eisenmenger's complex. In Cases 3 and 4 the degree of dextroposition is difficult to evaluate in view of the corrected anomaly.

3. The latter cases offer an interesting experiment of nature whereby one of the features of the malformation is totally or partially corrected. This peculiarity supports the view that vascular changes in the lungs seem to originate as a consequence of the biventricular origin of the aorta and not as a congenital vascular anomaly. If this view is correct, the explanation lies in the fact that a right ventricle must elevate its pressure to a considerable degree when it faces systemic resistances.

4. Histologic studies in Cases 1 and 2 justify our belief in the elevation of pressure within the pulmonary circuit as the sole cause for vascular pathology

in the lungs. As a counterproof to this statement, Case 3 shows that these vascular changes do not occur when the aorta does not have a double ventricular origin, in spite of its dextroposition.

5. Cyanosis was not present in our cases. This is most remarkable in Case 2, where cyanosis might have seemed inevitable. This seems to indicate that permanent cyanosis in Eisenmenger's complex (at least visible cyanosis) is a late phenomenon and it is otherwise seen as a terminal occurrence. It also points out the importance of an adequate blood supply to the lungs to avoid the appearance of visible cyanosis, and the relatively slight importance of a dextroposed aorta, as concerns this symptom.[8,10]

6. Rapidly progressive heart failure of sudden onset is a common feature in three of our cases.

7. The diagnosis was not established in life. Some of the features in these cases are compatible with Eisenmenger's complex, but these are not strongly suggestive. Moreover, one case led to the erroneous diagnosis of patent ductus arteriosus due to the presence of misleading features. It would seem, in view of the findings at the autopsy, that the presence of a right aortic arch as in Case 1 and perhaps in Case 2, should aid in the differential diagnosis. The literature consulted indicates that atypical cases are rather common, such as Baumgartner and Abbot's,[19] Millman and Kornblum's,[24] Bond's,[23] Taussig and Semans',[16] and Hurst and Schemm's,[15] especially in the presence of an added aortic insufficiency.[25]

SUMMARY

Four atypical cases of Eisenmenger's complex are studied clinically and pathologically. Two show a spontaneous occlusion of the ventricular septal defect by total or partial attachment of the septal leaflet of the tricuspid to the septum. An interesting experiment of nature is thus produced, substantiating the views that pulmonary vascular changes are not congenital but a consequence of the biventricular origin of the aorta, causing right ventricular pressure elevation as proved by histologic studies in Cases 1 and 2. Conversely, Case 3 has no vascular changes since the aorta is not biventricular although dextroposed.

Cyanosis was absent in all cases; adequate lung blood supply explains its absence despite aortic dextroposition. Rapidly progressive heart failure of sudden onset was a common feature in three cases. The correct diagnosis was missed antemortem. The presence of a right aortic arch should be a useful diagnostic aid.

SUMMARIO IN INTERLINGUA

Es presentate un studio clinic e pathologic de quatro casos atypic del complexo de Eisenmenger. Duo exhibiva occlusion spontanee del defecto ventriculoseptal per le attachamento partial o total del folietto septal del valvula tricuspide al septo. Iste casos representa un interessante "experimento del natura" que supporta le these que alterationes pulmono-vascular non es congenite sed consequentias del origine biventricular del aorta, causante un elevation del pression dextero-ventricular (como demonstrate per studios histologic in casos 1 e 2). Del altere latere, caso 3 exhibiva nulle alterationes vascular proque le aorta non esseva biventricular ben que dexteroponite.

Cyanosis esseva absente in omne le quatro casos. Un adequate apporto pulmonar de sanguine explica le absentia de cyanosis in despecto del dextero-position. Como characteristica commun de tres casos nos observava disfallimento cardiac de declaration subitanee e progresso rapide. Le correcte diagnose non esseva establite ante morte. Le presentia de un arco dextero-aortic es probabilemente un importante adjuta diagnostic.

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EVIDENCE FOR HEART DAMAGE IN ASSOCIATION WITH SYSTEMIC HYPOTHERMIA IN DOGS

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THE possibility of damage to vital structures by induced hypothermia in animals and humans has not been solved definitively. The occurrence of visceral congestion, ascites, and subendocardial hemorrhages in dogs subjected to hypothermia has been reported.[1-5] However, no special significance has been attached to these pathologic findings, and it seems to be generally accepted by most investigators that systemic hypothermia, as it is used in modern cardiac surgery, is a noninjurious and rather safe procedure. In our opinion this view is not based on systematic investigations. At the same time, the mechanism of hypothermic, posthypothermic, and so-called rewarming death has not been satisfactorily explained. For these reasons, and in order to elucidate further the value of various medical applications of hypothermia, systematic studies on the pathology of hypothermia are necessary.

Our recent study,[6] in which a number of dogs were autopsied in different stages of cooling or immediately at the termination of rewarming, revealed pathologic-anatomic changes of visceral congestion, ascites, and subendocardial hemorrhages noted by others. In addition, histologic evidence of injury to the heart, liver, and brain was observed. The histologic changes noted in the heart muscle consisted principally of areas of hyaline necrosis with an occasional cellular reaction and of some "degenerative changes." Since the material was too small to warrant definite conclusions, further study of this problem was deemed necessary.

One could conclude that the afore-mentioned myocardial changes, if true, represent only the early stages of vital reactions which result in more marked myocardial changes, later on. Therefore, the present study was particularly intended to elucidate the pathology of the heart in dogs subjected to controlled hypothermia and sacrificed at varying intervals following survival.

MATERIAL AND METHODS

The material consisted of twenty-four apparently healthy dogs, unselected as to breed, age, or sex, and weighing from 5.3 to 18.5 kilograms. They were

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anesthetized with intravenous Nembutal (25 mg. per kilogram), heparinized (2.5 mg. per kilogram), and intubated. Thereafter, they were cooled in an ice bath (4° to 8° C.). With few exceptions, artificial respiration was used. During immersion, small amounts of ether, sufficient to prevent shivering, were administered. For both purposes the AGA-Crafoord spiropulsator was used. In one case a "Cocktail lytique" supplemented with Nembutal (15 mg. per kilogram)[7] was used for anesthesia. Dog 24 was cooled by use of extracorporeal circulation and disk oxygenator ad modum Juvenelle and associates.[5]

Nine dogs were autopsied immediately after fatal cardiac crisis or at the termination of moderate (26° to 27.5° C.) or deep (21° to 22.5° C.) hypothermia of one to four hours' duration. Fifteen dogs were sacrificed and autopsied three days to three years after they had survived a moderate or deep hypothermia of the same duration. The details of the cooling procedures in the different cases appear in Table I.

The hearts were studied in detail, grossly and histologically. Sections of all portions of the left and right sides of the heart, including the anterior, posterior, and apical portions of both ventricles, the papillary muscles of the left ventricle, the interventricular septum, and of the atria were examined histologically. The material was fixed in 10 per cent Formalin and stained with scarlet red and hemalum-eosin.

OBSERVATIONS

Evidence of intrinsic myocardial damage in dogs autopsied at different stages of cooling and at varying intervals after they had survived the state of controlled hypothermia appears in Table I. The data of myocardial alterations presented in this table reveal distinct differences in the gross and histologic appearance of the lesions in these two groups.

In the former group, i.e., in dogs autopsied immediately after fatal cardiac crisis or at the termination of prolonged hypothermia, the myocardial changes, except subendocardial hemorrhages, could be detected only by careful histologic examination. The most typical pathologic feature in this group was the occurrence of necrotic muscle fibers in the myocardium. These were found in all nine dogs of this group. Signs of necrosis, mainly hyalinization of the cytoplasm with concomitant pyknosis of nuclei, occurred in single fibers or in groups of fibers (Figs. 3 and 4), which in some instances were widely distributed throughout the myocardial wall (Fig. 2*a*). In seven of nine cases (Dogs 1 to 5, 7, and 8) such affected areas showed early reactive cellular phenomena (Figs. 1*a* to 3). The infiltrating cells were mainly lymphocytes or lymphocyte-like cells, but occasionally a few polymorphonuclears, mesenchymal cells, and Anitschkow myocytes were present (Figs. 1*a* and 1*b*). Another pathologic feature in these dogs was the presence of fatty degeneration of the myocardium. In particular, it was most apparent in the dogs which were autopsied at the termination of prolonged periods of moderate or deep hypothermia (Dogs 3, 4, 6, 7, and 8).

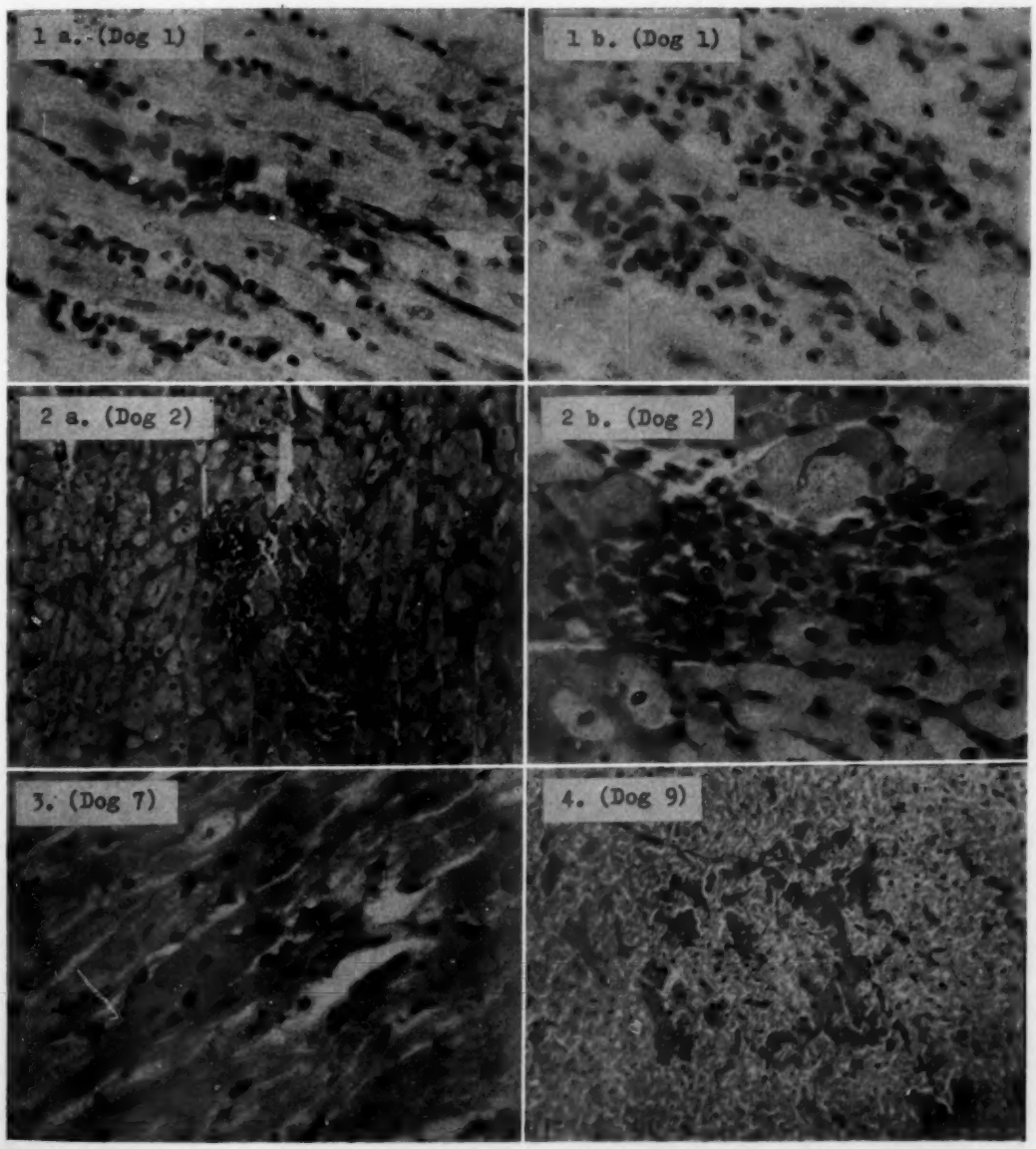
The myocardial alterations noted in dogs sacrificed at various intervals after survival of the cooling procedure differed strikingly from those seen in the former group. In thirteen of fifteen cases of this group there were distinct lesions

TABLE I. DATA OF COOLING PROCEDURES, THE POINTS OF AUTOPSY, AND MYOCARDIAL CHANGES IN ASSOCIATION WITH SYSTEMIC HYPOTHERMIA IN DOGS

DOG NO.	ANESTHESIA	RESPIRATION	CHARACTERISTICS OF HYPOTHERMIA (C.)	REWARMING	AUTOPSY	MYOCARDIAL CHANGES
1	N + E	Artif.	Fatal termination at 17.7°	—	15 hours later	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells and a few mesenchymal cells (Figs. 1*a* and 1*b*)
2	N + E	Artif.	Fatal termination at 17.0°	—	Immediately	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells and a few mesenchymal cells (Figs. 2*a* and 2*b*)
3	N + E	Artif.	1 hour at 21–22.5°	—	Immediately	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells and a few mesenchymal cells. Wide areas of fatty degeneration
4	N + E	Artif.	2 hours at 21–22.5°	—	Immediately	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells. Wide areas of fatty degeneration
5	N + E	Artif.	4 hours at 21–22.5°	—	Immediately	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells
6	N + E	Artif.	4 hours at 21–22.5°	—	Immediately	Necrotic muscle fibers without evident cellular reaction. Rather patchy type of fatty degeneration
7	N + E	Spont.	4 hours at 26–27.5°	—	Immediately	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells (Fig. 3). Rather patchy type of fatty degeneration
8	N + E	Artif.	4 hours at 26–27.5°	—	Immediately	Necrotic muscle fibers occasionally surrounded by lymphocyte-like cells. Rather diffuse type of fatty degeneration
9	C.l. + N	Spont.	4 hours at 26–27.5°	—	Immediately	Necrotic muscle fibers without evident cellular reaction (Fig. 4)
10	N + E	Artif.	1 hour at 21–22.5°	+	5 days later	Small foci of necrosis infiltrated by mesenchymal cells
11	N + E	Artif.	2 hours at 21–22.5°	+	7 days later	Small foci of necrosis infiltrated by mesenchymal cells
12	N + E	Artif.	4 hours at 21–22.5°	+	3 days later	Small foci of necrosis infiltrated by mesenchymal cells
13	N + E	Artif.	4 hours at 21–22.5°	+	4 days later	Necrotic foci of varying size infiltrated by mesenchymal cells. Partly calcified and grossly visible. Beginning collagen formation
14	N + E	Artif.	4 hours at 21–22.5°	+	4 days later	Necrotic foci of varying size infiltrated by mesenchymal cells (Figs. 5*a* and 5*b*). Partly calcified and grossly visible
15	N + E	Artif.	5 hours at 21–22.5°	+	4 days later	Necrotic foci of varying size infiltrated by mesenchymal cells (Fig. 6). Grossly visible
16	N + E	Artif.	4 hours at 21–22.5°	+	14 days later	No distinct myocardial changes
17	N + E	Artif.	4 hours at 21–22.5°	+	14 days later	Necrotic foci of varying size infiltrated by mesenchymal cells. Partly calcified and grossly visible. Prominent collagen formation (Figs. 7*a*, 7*b*, and 7*c*)
18	N + E	Artif.	4 hours at 21–22.5°	+	14 days later	Necrotic foci of varying size infiltrated by mesenchymal cells. Partly grossly visible. Prominent collagen formation
19	N + E	Artif.	4 hours at 21–22.5°	+	14 days later	Necrotic foci of varying size infiltrated by mesenchymal cells. Partly calcified and grossly visible. Prominent collagen formation
20	N + E	Artif.	4 hours at 21–22.5°	+	14 days later	No distinct myocardial changes
21	N + E	Artif.	4 hours at 26–27.5°	+	4 days later	Necrotic foci of varying size infiltrated by mesenchymal cells. Party calcified and grossly visible (Figs. 9*a* and 9*b*)
22	N + E	Artif.	4 hours at 26–27.5°	+	4 days later	Small foci of necrosis infiltrated by mesenchymal cells
23	N + E	Artif.	4 hours at 26–27.5°	+	3 days later	Necrotic areas of varying size infiltrated by mesenchymal cells (Fig. 8). Partly grossly visible
24	P	Artif.	Cooling to 12° with an immed. rewarming. Extracorp. circ. and disk oxygenator were used	+	3 years later	Grossly visible fibrotic scars with heteroplastic bone formation

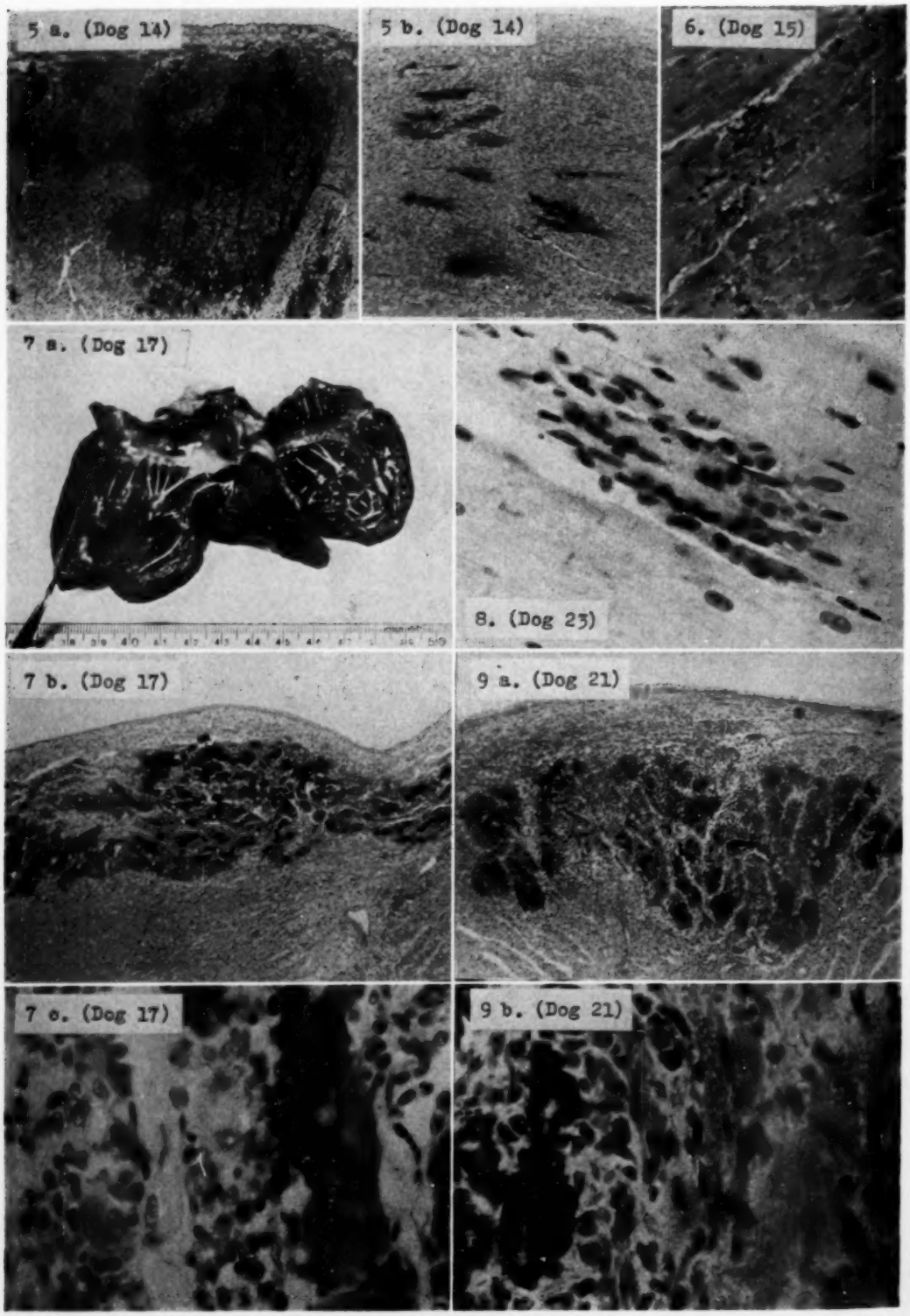
Abbreviations: N = Nembutal; E = Ether; C.l. = "Cocktail lytique"; P = Pentothal.

in the myocardium, which were grossly recognizable in nine cases. The lesions generally consisted of isolated, disseminated, yellowish-gray foci of varying size (Figs. 7 *a*, 7 *b*, and 8). Histologic examination of these foci revealed well-defined calcified areas of necrosis, with an intense cellular reaction. The constituents of the infiltrating cells, as well as other characteristics of the histologic picture in the different cases, varied considerably, depending on the length of time from the cooling process to the point of sacrifice of the animal. In dogs



Figs. 1*a* to 4.—Myocardial changes in dogs autopsied at the onset of fatal cardiac crisis (Figs. 1*a* to 2*b*) or at the termination of moderate (26° to 27.5° C.) hypothermia of four hours' duration (Figs. 3 and 4). The muscle fibers show evident hyaline necrosis associated (Figs. 2*a* to 3) or not (Fig. 4) by early reactive cellular phenomena. In Figs. 1*a* and 1*b* there is cellular infiltration, but injury to the muscle fibers is less evident. See details in text and Table I.

Abbreviations: N = Nembutal; E = Ether; C.L. = "Cocktail lytique"; P = Pentothal
Oxygenator were used



Figs. 5*a* to 9*b*.—Areas of myocardial necrosis at different stages of development and healing in dogs held four to five hours at a rectal temperature of 26° to 27.5° C. or 21° to 22.5° C. The dogs were sacrificed and autopsied three to fourteen days following rewarming. Fig. 7*a* shows the typical gross appearance of the lesions within this survival time (light endocardial spots near the left ventricular apex and on the papillary muscles of the left ventricle). The other figures illustrate the histologic characteristics of the lesions. See details in text and Table I.

sacrificed and autopsied from three to seven days after the cooling process the infiltrating cells consisted predominantly of mesenchymal cells, which frequently showed mitotic figures (Fig. 9 *b*). Polymorphonuclear leukocytes, lymphocytes, and Anitschkow myocytes were rare or absent. Collagen formation, if present, was not prominent. In addition, the muscle fibers in the periphery of the necrotic foci often showed an intense fatty degeneration (Fig. 9 *b*). The gross appearance of the myocardial lesions in dogs sacrificed and autopsied fourteen days after the cooling process was essentially the same. Histologically, however, there was prominent collagen formation, and definite plasma cells, giant cells, and pigmented macrophages were noted among the infiltrating cells (Fig. 7*c*). Finally, the myocardium of the dog (Dog 24) which was sacrificed and autopsied three years after it had survived a deep hypothermia, showed well-defined, contracted fibrotic scars with heteroplastic bone formation.

The localization of the myocardial changes summarized above was the same in all dogs. The lesions were restricted to the walls of the right and left ventricle, whereas the atrial walls were characteristically intact. Although the lesions could be detected in any portion of the ventricles, the apical portions (Figs. 7 *a*, 7 *b*, and 7 *c*), the papillary muscles of the left ventricle (Fig. 5 *b*), and the anterior wall of the right ventricle including the adjacent areas of the pulmonary conus (Figs. 5 *a*, 9 *a*, and 9 *b*) disclosed abnormalities with somewhat greater frequency. The lesions were located for the most part subendocardially (Figs. 7 *a*, 7 *b*, and 7 *c*), but could also be found beneath epicardium (Figs. 5 *a* and 9 *a*). In both instances, however, there was always a thin layer of surviving myocardium along the endocardial and epicardial surfaces.

DISCUSSION

It is evident that the myocardial alterations detected in twenty-two of twenty-four cases are of pathologic nature and that the lesions in some way are related to the cooling procedure. Every necrobiotic process naturally arises from a variety of noxae. However, from the etiologic point of view, it is of interest that the myocardial changes found during cooling and at various intervals following survival, grossly and histologically correspond to the known successive stages in the development and healing of experimental infarctions in dogs.[8,9] There was always a thin layer of surviving myocardium just beneath the endocardium and epicardium. This phenomenon is also characteristic of infarctions in animals and humans[9,10] and has been related to the more efficient Thebesian circulation and collateral blood supply of the subendocardial and subepicardial muscle layers respectively.[11] These data furnish evidence for the view that the lesions in our dogs are possibly due to focal disturbances in the myocardial blood supply rather than to a systemic anoxemia or hypoxemia. Whether these lesions actually are true infarctions or not remains unresolved for the present. However, the occurrence of micro-embolisms in hypothermic dogs has been demonstrated[12] and in our dogs some narrowing processes of an apparently inflammatory nature were frequently seen in the myocardial arterioles. These observations suggest that the lesions found in our dogs are true infarctions. This is further supported by the fact that the lesions mainly were focal in nature

and rather sharply delineated. However, it must be born in mind that even hypoxemic states of different nature, as well as relative myocardial hypoxia, may result in patchy myocardial lesions[13,14] and that at the present time there are no striking arguments against the possibility of myocardial hypoxia in hypothermic dogs. For example, the observation in dogs that the coronary arteriovenous oxygen difference remains unchanged with rectal temperatures as low as 17° C.[15] does not necessarily indicate adequacy of the myocardial oxygen supply.

The functional significance of the lesions detected in our dogs will not be discussed in detail. However, it is possible that the myocardial changes described above may lead to conduction disturbances, ectopic rhythms, and myocardial insufficiency. These, in turn, may result in fatal cardiac failure, particularly in the presence of other physiologic changes associated with the cooling and rewarming process or trauma to the heart directly, as in cardiac surgery.

SUMMARY

Twenty-four dogs were subjected to systemic hypothermia. Nine dogs were autopsied at the onset of fatal cardiac irregularities or at the termination of moderate (26° to 27.5° C.) or deep (21° to 22.5° C.) hypothermia of one to four hours' duration. In all cases the myocardium showed foci of necrotic muscle fibers with an occasional cellular reaction. Fifteen dogs were sacrificed and autopsied three days to three years after survival of moderate or deep hypothermia of the same duration. In thirteen of fifteen cases distinct areas of necrosis showing various stages or organization were detected. The nature and the etiology of the lesions as well as their functional significance are discussed.

SUMMARIO IN INTERLINGUA

Vinti-quatro canes esseva subjicite a hypothermia systemic. Ex illos, 9 esseva autopsiate al declaration de mortal irregularitates cardiac o al termination de cursos de 1 a 4 horas de hypothermia moderate (26 a 27, 5 C) o profunde (21 a 22,5 C). In omne casos le myocardio revelava focos de necrotic fibras muscular e sporadic reactiones cellular. Dece-cinque canes esseva sacrificate e autopsiate post superviver a moderate o profunde hypothermia del grados e durationes mentionate pro periodos de inter 3 dies e 3 annos. In 13 del 15 casos, areas distincte de necrosis in varie phases de organisation esseva detegite. Es discutite le natura e le etiologia del lesiones e etiam lor signification functional.

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PRESSURE CURVES FROM THE CORONARY SINUS OF THE DOG

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ONLY a few investigators have reported and described coronary sinus pressure tracings. Their curves exhibited no consistency either as to absolute pressure values or as to wave form. The relationships of either the pressure values or wave pattern to other hemodynamic factors or events occurring in the cardiovascular system have been virtually ignored. The present report describes various wave patterns recorded from the coronary sinus of the anesthetized dog and attempts some correlation with other simultaneously recorded phenomena.

METHODS

Fifty-six experiments were conducted on thirty-eight adult mongrel dogs having a mean body weight of 18.4 kg. The animals were anesthetized with an intravenous injection of 30 mg. pentobarbital sodium per kilogram body weight, and then heparinized, 5 mg. heparin per kilogram body weight. Under fluoroscopic visualization, catheters were placed in the coronary sinus, the main pulmonary artery, and, occasionally, in the right ventricle. A plastic cannula was inserted into a branch of the femoral artery. Electrocardiographic tracings, usually aV_F, were obtained simultaneously with continuous blood pressure recordings, by means of Statham pressure transducers and Sanborn amplifiers and recorders. Calibration of the transducers and determination of the frequency response of the system were performed at frequent intervals.

Confirmation of the position of the various catheters was obtained at the end of the experiment by fluoroscopic visualization and, in a number of instances, at autopsy. The coronary sinus catheter was always placed 1 to 2 cm. inside the ostium. Additional evidence that the catheter had successfully entered the coronary sinus was given by the low oxygen content of the coronary venous blood.

The pressure curves utilized in this study were recorded approximately one hour after the animal was anesthetized. The analysis of the data obtained was devoted primarily to the contour of the pressure curves and their absolute pressure values. Further relationships were investigated by reference to curves obtained from other portions of the vascular bed and to the electrocardiogram.

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The availability of other hemodynamic data, such as cardiac output, coronary blood flow, and coronary and systemic vascular resistances permitted certain correlations to be made. Coronary vascular resistance (CVR) was measured by dividing the difference between the mean arterial pressure and the mean coronary pressure (both in mm. Hg) by coronary blood flow in milliliters per 100 Gm. per minute.

All data were subjected to a statistical analysis. Wherever adequate data were available, they were correlated with the coronary sinus pressures. The null hypothesis was rejected at the 5 per cent level.

RESULTS

Pressures.—The data are summarized in Table I. The venous systolic pressure in the coronary sinus of the anesthetized dog averaged 6.1 mm. Hg, while the diastolic pressure was 1.9 mm. Hg. The values for the pulse and electronically integrated mean pressures were 3.8 and 3.3 mm. Hg, respectively. The integrated mean pressure was approximately 0.1 mm. Hg lower than the calculated arithmetical mean. Respiration induced profound changes in coronary sinus pressure values. During inspiration the pressure fell precipitously, 1 to 2 mm. Hg below the base line, while it rose sharply by a similar amount in expiration. Pressure values recorded were measured during the expiratory pause of the respiratory cycle. The pressure values from the femoral artery, the pulmonary artery, and the right ventricle approximated closely those reported by previous investigators.[1]

TABLE I. SIMULTANEOUS PRESSURES IN MM. HG FROM VARIOUS PARTS OF THE VASCULAR BED

	NUMBER OF OBSERVATIONS	MEAN	S.D.*	S.E.†
Coronary sinus				
Systolic	56	6.1	2.53	0.338
Diastolic	56	1.9	2.67	0.356
Mean‡	56	3.3	3.21	0.429
Pulse pressure	56	3.8	2.65	0.354
Pulmonary artery				
Systolic	41	15.3	7.00	1.095
Diastolic	41	8.1	5.34	0.834
Mean‡	41	10.5	5.68	0.887
Right ventricle				
Systolic	11	17.5	6.52	1.965
Diastolic	11	−3.1	2.45	0.745
Mean‡	11	5.0	2.18	0.659
Femoral artery				
Systolic	53	155	9.86	1.354
Diastolic	53	112	6.31	0.867
Mean‡	53	125	7.23	0.993

*Standard deviation.
†Standard deviation of the mean.
‡Electronically integrated.

Correlations.—A significant correlation ($r = 0.825$, $p < 0.001$) was observed between coronary sinus diastolic and right ventricular end diastolic pressures. A low though significant correlation was found between all pulmonary pressures and coronary sinus diastolic and mean pressures (Table II). A low correlation was observed between mean coronary sinus pressure and coronary flow in the left ventricle (Table III). The data on other correlations are being reported in a separate communication.[2]

TABLE II. CORRELATIONS BETWEEN MEAN, SYSTOLIC, AND DIASTOLIC PRESSURES IN THE CORONARY SINUS AND OTHER POINTS IN THE CARDIOVASCULAR SYSTEM

	NUMBER OF OBSERVATIONS	CORRELATION COEFFICIENT	STANDARD ERROR OF THE CORRELATION COEFFICIENT	PROBABILITY
Coronary Sinus—Mean				
Arterial Systolic	53	0.121	0.135	0.4–0.3
Diastolic	53	0.067	0.136	> 0.5
Mean	53	0.093	0.136	0.5–0.4
Pulmonary Systolic	41	0.386	0.133	0.004
Diastolic	41	0.301	0.142	0.034
Mean	41	0.322	0.140	0.021
Rt. Ventricular Systolic	11	0.120	0.299	> 0.5
Diastolic	11	0.386	0.258	0.2–0.1
Mean	11	0.345	0.267	0.3–0.2
Coronary Sinus—Systolic				
Pulmonary Systolic	41	0.322	0.140	0.021
Diastolic	41	0.266	0.148	0.2–0.1
Mean	41	0.241	0.147	0.1
Rt. Ventricular Systolic	11	0.245	0.285	0.5–0.4
Diastolic	11	0.466	0.237	0.050
Mean	11	0.088	0.301	> 0.5
Coronary Sinus—Diastolic				
Pulmonary Systolic	41	0.300	0.142	0.035
Diastolic	41	0.324	0.140	0.021
Mean	41	0.311	0.141	0.027
Rt. Ventricular Systolic	11	0.123	0.298	> 0.5
Diastolic	11	0.825	0.097	0.001
Mean	11	0.374	0.261	0.2–0.1

Pressure curves.—The coronary sinus pressure curves contained the three essential venous waves; a, c, and v, respectively. Frequently, however, successive waves were merged together or obliterated, causing the contour of the coronary sinus pressure curve to approach the wave forms observed in the aorta, pulmonary artery, right ventricle, or right atrium. The various inflections of the simple venous wave exhibited the larger pressure values at different times.

The a-wave had a rounded or somewhat spiked shape. The pressure rose to a maximum, but, with the commencement of auricular relaxation, it fell to a variable extent. In some records, the pressure at this time was higher than at the onset of auricular systole; in others, it was equal or less. The c-wave first reached a peak during the period of ventricular systole and then decreased to attain its lowest value late in diastole. A v-wave of varying amplitude followed.

Occasionally, a small vibration attributed to the closure of the semilunar valves appeared on the upstroke of this wave. The decline of the pressure occurred quite rapidly; however, the extent of the fall varied considerably.

An attempt has been made to place tracings with general points of resemblance into common groups. A careful examination of all the records obtained suggested the possibility of five fundamental forms of coronary sinus pressure curves. These have arbitrarily been designated as Types I, II, III, IV, and V (Fig. 1).

TABLE III. CORRELATIONS BETWEEN MEAN CORONARY SINUS PRESSURES AND SOME MEASURES OF CARDIAC FUNCTION AND ACTIVITY

	NUMBER OF OBSERVATIONS	CORRELATION COEFFICIENT	STANDARD ERROR OF THE CORRELATION COEFFICIENT	PROBABILITY
Cardiac output (L./min.)	41	0.197	0.150	0.2–0.1
Heart rate (beats/min.)	56	−0.026	0.133	> 0.5
Coronary flow/100 Gm. L.V./min.	41	0.033	0.156	> 0.5
Coronary flow/L.V./min.	42	0.286	0.141	0.04
Arterial O_2 (vol. %)	50	0.169	0.137	0.3–0.2
Arterial CO_2 (vol. %)	21	0.224	0.206	0.3–0.2
Coronary venous O_2 (vol. %)	48	0.256	0.135	0.05
Coronary venous CO_2 (vol. %)	22	0.160	0.207	0.5–0.4
O_2 consumption L.V. (ml./min.)	42	0.153	0.150	0.3–0.2
Coronary vascular resistance	36	0.031	0.166	> 0.5

Type I curves were characterized by comparatively smooth contours and rounded arched summits. They had the general form of atrial pressure curves. Tracings having this contour were obtained in 16 per cent of the records. The curves showed three successive inflections. The a-wave was the most prominent curve in Type I tracings. The rise and fall of this curve occurred without vibrations. The summit consisted of an arch, the geometrical form of which varied considerably. The c-wave was also free from vibrations and smaller in amplitude than the a-wave. The v-wave was always present in Type I curves.

Type II curves had a contour very similar to an aortic pressure wave. They were devoid of the decisive inflections present in Type I. Only a single peak occurred, synchronously with the onset of ventricular systole. The curve generally rose steeply and smoothly to a rounded summit. The v-wave occurred as a small vibration somewhere on the catacrotic limb, during the S-T segment of the electrocardiogram. It was most evident when the heart rate was slow. The trough of the curve was reached during auricular contraction. Such "aortic" curves were detected in 14 per cent of the sample.

Type III curves occurred in 50 per cent of the records. They were chiefly characterized by a large v-wave. The a-wave was usually absent from Type III curves, although in some instances, it could be detected as a slight vibration low on the catacrotic limb of the v-wave. A small c-wave inaugurated tracings of this type. In some records, the c-wave was a discrete inflection, but in others

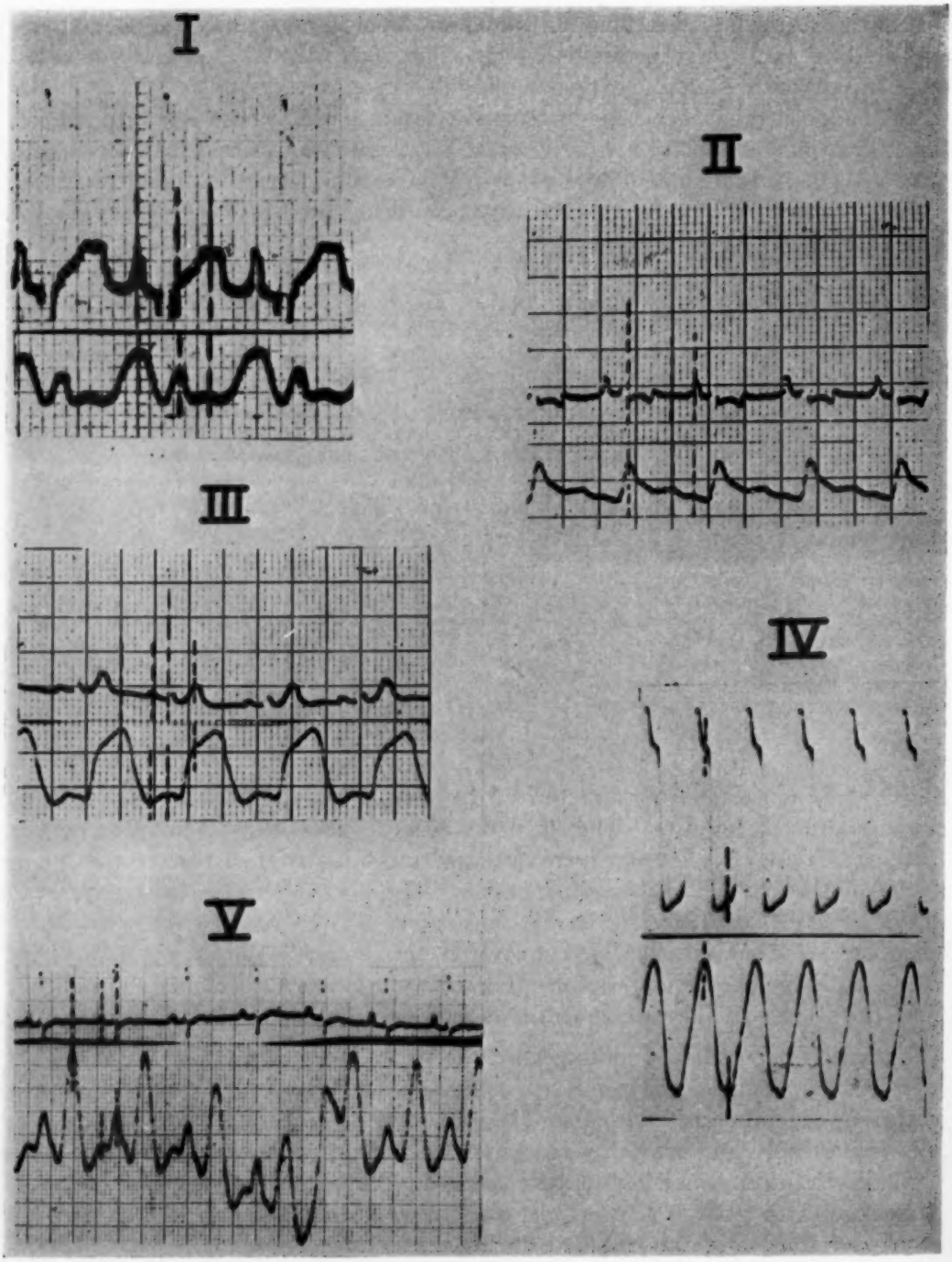

Fig. 1.—Pressure curves from the coronary sinus of the anesthetized dog. I, II, III and V represent coronary sinus curves synchronously obtained with electrocardiographic Lead aV_F, while IV is a synchronous record of coronary sinus and left ventricular pressure waves. Alignment marks relate various events. Type I illustrates a typical atrial-like curve. Type II similarly illustrates an aortic-like curve. The dominant v-wave and the absence of an a-wave is typical of Type III curves. Type IV curves simulate right ventricular tracings. Type V curves are similar to those in Type I, except that the v-wave is most prominent. The influence of respiration is well illustrated in this tracing. The coronary sinus pressure wave is the lower tracing in all the records.

it was merged with the following large v-wave, producing a shoulder near the base line or an incisura high on either the anacrotic or the catacrotic limb. The location of this incisura depended upon whether the peak of the v-wave occurred early or late in diastole. The smooth v-wave rose steeply to a rounded or peaked crest, except for a short inflection which appeared midway on the ascending limb coincidentally with the T wave of the electrocardiogram. The decline of the v-wave proceeded without interruption, rapidly at first, and then more slowly. In some instances, Type III curves approached the essential features of pulmonary arterial waves.

Type IV curves had a very simple contour, resembling right ventricular waves. The curve first rose steeply and uninterruptedly to a high level, the peaked or plateaulike summit being coincident with the protodiastolic period of ventricular activity. The decline was rapid and free from vibrations. The trough was reached late in auricular systole, and was characteristically marked by an abrupt depression below the base line. No other inflections were present in Type IV curves, which occurred in only 5 per cent of the records.

Type V curves were characterized by the fact that their contour exhibited the inflections characteristic of Type I curves, but differed from those in that the v-wave was most prominent. The a-wave was marked, and ended at a level of pressure higher or lower than that seen at the commencement of the cycle. The c-wave ascended variably to a peak. It was followed by a negative depression, which continued to the base line, ending simultaneously with the T wave of the electrocardiogram. The tracing then exhibited a rise during diastole, leading to the high v-wave. Some variation in gradient was observed in relation to both limbs, but these were characteristically free from vibrations. The trough was reached just before the onset of atrial systole. Type V curves were encountered in 15 per cent of the records.

There was no relationship between these various pressure patterns and the absolute pressure values recorded.

DISCUSSION

The few investigators who have described coronary sinus pressure curves do not agree as to their exact contour or their absolute pressure values. Gregg[3] reported in dogs a tracing similar to a right atrial pressure curve. The systolic rise was largely missing and a pressure wave, coincident with the time of auricular systole, was evident. Goodale and associates[4] also published a "typical" coronary sinus pressure wave resembling a dampened atrial wave. Culbertson and associates[5] obtained and described four types of variations of pressure tracings from the coronary sinus of four men, while Bing and associates[6] found two types of curves; one resembled closely a right atrial tracing and the other a dampened aortic wave. Subsequently, Bing[7] presented an exceedingly simple curve, consisting of only one peak occurring just after the peripheral arterial systolic peak, and subject to marked respiratory fluctuations. Miller and associates[8] described a variety of forms of pressure curves from the coronary sinus of patients. The curves presented by Soulie and associates[9] and Eckstein and associates[10] could not be adequately evaluated due to poor definition of their shape.

The pressure waves obtained from the coronary sinus were exceedingly variable not only in different animals but frequently in the same animal during the course of an experiment. Consequently, even the present attempt to classify wave forms into several categories cannot be considered a satisfactory solution. The aortic head of pressure and the resistance to flow which, in turn, is dependent upon the degree of contraction of the intrinsic muscles of the coronary vessels, the extent of extravascular compression or support of these vessels, the viscosity of the blood, the volume-elastic effects produced by the pulsating atrial pressure, and the degree of fullness of the bed are undoubtedly major factors, the variation of which resulted in the complex and changing form of coronary sinus pressure waves. The contour of the curve and the pressure values obtained cannot be utilized alone in confirming the location of a catheter in the coronary sinus. Presumably, a number of common factors are concerned in the production of a certain wave form, but the present data are not adequate for elucidation. Additional studies are being attempted in the hope that a cause-and-effect relationship can be demonstrated.

The coronary sinus pressure values recorded by previous investigators, both in dogs[3,4] and men,[5-7] were considerably higher than those obtained in the present series. It is probable that the high pressures were occasioned by the location of the catheter deep in the coronary venous system where it could occlude a portion of the bed. Such occlusion was not present in the experiments reported herein, as evidenced by the consistently low pulse pressures, the level of the absolute pressures, and the ease with which coronary venous blood samples were obtained.

The highly significant correlation between coronary sinus diastolic and right ventricular end diastolic pressures was not unexpected and simply confirmed the anticipated static state of the entire right heart at this particular moment of the cardiac cycle. However, the relationships between all pulmonary pressures and coronary sinus diastolic and mean pressures were unexpected. Although the coefficients of correlation were small, they were nonetheless significant. No explanation for these findings can be given, though it is interesting to speculate that there may be some connection with the pulmonary-coronary reflexes reviewed by Dawes and Comroe.[11] The observed relation between coronary sinus mean pressure and total blood flow through the left ventricle confirmed the findings of others,[6] but it should be noted that the correlation was low even though significant. Many other correlations in addition to those listed in Tables II and III were made, but none were found to be significant. Other investigators[12] have reported correlations with some of those attempted by the present authors, but in general their data have not been extensive and the correlations found were low.

SUMMARY

Pressure curves recorded from the coronary sinus (at a depth of 1 to 2 cm.) of fifty-six anesthetized dogs were analyzed in respect to their absolute values and general contours. The relationship of pressure values to certain hemodynamic factors and events occurring in the cardiovascular system was investigated. Pressures in the coronary sinus were low, 6.1 and 1.9 mm. Hg for systolic and diastolic values, respectively. A statistically significant correlation was found between coronary sinus diastolic and right ventricular end diastolic pres-

sures. Lower correlations were obtained between coronary sinus diastolic and mean pressures and all pulmonary pressures, as well as between coronary sinus mean pressure and total left ventricular blood flow. The pressure curves recorded were extremely variable, not only in different animals, but in the same animal during the course of an experiment. Although it was possible to group these pressure tracings into five major patterns, considerable variation was observed within each main type.

SUMMARIO IN INTERLINGUA

Curvas de pression, registrate ab le sinus coronari (a un profunditate de 1 a 2 cm) in 56 canes anesthesiate esseva analysate relative a lor valores absolute e lor contornos general. Esseva investigate le relation del valores de pression con certe factores e evenimentos hemodynamic in le systema cardiovascular. Le pressiones in le sinus coronari esseva basse, 6,1 mm Hg systolic e 1,9 mm Hg diastolic. Esseva constatate un statisticamente significative correlation inter le pressiones coronario-sinusal diastolic e dextero-ventricular diastolic terminal. Plus basse correlationes esseva observate inter le pressiones coronario-sinusal diastolic e median e omne pressiones pulmonar e etiam inter le pression coronario-sinusal median e le total fluxo sanguinee sinistro-ventricular. Le curvas de pression esseva extrememente variabile, non solmente in varie animales sed etiam in le mesme animal in le curso de un sol experimento. Ben que il esseva possibile classificar le registrationes de pression in cinque typos de configuration, le variationes intra omne typo esseva considerabile.

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Clinical Report

ANEURYSM OF RIGHT SINUS OF VALSALVA WITH RUPTURE INTO RIGHT ATRIUM AND INTO THE RIGHT VENTRICLE

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ANEURYSMS of the sinuses of Valsalva, while always unusual, are being recognized with some degree of frequency in recent years. The reporting of the syndrome produced by a rupture has revived the interest that was once aroused many years ago by Thurmans' original report.[1]

Isolated cases of rupture of a sinus of Valsalva into the right atrium, to mention a few, were described by Charcot[2] in 1860, by Higgins[3] in 1934, by Wright[4] in 1937, by Russell and Thompson[5] in 1945, by Tenczar et al.[6] in 1951, and by Venning[7] in 1951.

The purpose of this paper is to report a case of a congenital aneurysm of the right sinus of Valsalva that ruptured into the right atrium and into the right ventricle. A correct antemortem diagnosis was made at the bedside before cardiac catheterization studies were carried out. Another interesting feature was the presence of a subacute bacterial endocarditis with rupture of an aortic leaflet.

CASE REPORT

A 19-year-old American-born Negro woman was admitted to Cook County Hospital with complaints of swelling of the ankles and shortness of breath. She was in excellent health until ten days prior to admission, when she noted a gradual onset of swelling of the ankles and legs. At the same time she also noted sudden shortness of breath on climbing a single flight of stairs. Cough appeared which was productive of about one tablespoonful of white sputum daily. Edema initially subsided with rest but reappeared with activity and became progressive in severity. For two days prior to entry, the patient had noted swelling of the eyelids upon arising. The patient denied having pain or discomfort in the chest before or during this illness.

Systemic review revealed no orthopnea or paroxysmal nocturnal dyspnea. She had noted no chills, but was aware of some fever, with increased perspiration, especially at night. She had lost a slight, but indeterminate, amount of weight. There had been no hemoptysis, palpitations, or gastrointestinal complaints apart from anorexia during the week prior to entry. The patient had no neurological complaints. Her last menstrual period, normal in character and duration, had occurred ten days prior to admission.

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Past Medical History.—The patient had tonsillitis on several occasions in the distant past; no known allergies; venereal infection was denied, as was previous surgery. For one year prior to admission the patient had been treated for complaints of lower abdominal pain with a proprietary medicine said to be for a kidney ailment.

Personal History.—The patient had been born in Mississippi where she worked as a corn and cotton picker and as a laundry worker. She had arrived in Chicago eight months prior to her present illness, and had not been employed. She drank alcohol only occasionally and smoked ten cigarettes a day. Diet was questionably adequate.

Family History.—Family history was noncontributory; both parents were living and well.

Physical Examination.—Physical examination revealed a mildly ill, mentally dulled, restless patient in no distress. Blood pressure was 170/75/0 mm. Hg; pulse 120, regular and bounding; respirations 25 per minute; temperature 100° F. There was no periorbital edema or conjunctival pallor. Pupils reacted normally and the fundi appeared normal. There were no petechiae in the mouth or pharynx; tonsils were small and normal in appearance; the teeth appeared carious. Neck veins were moderately distended, and visible arterial pulsation was present in the suprasternal notch. The thyroid gland was not palpable, the trachea was in the midline, and no masses or nodes were palpable in the neck. The breasts were normal. Examination of the lungs revealed diffuse expiratory wheezes and rhonchi, and signs at the right lung base and in the right axilla, of dullness, diminished breath sounds, and vocal resonance.

The cardiac apex beat was forceful and well localized to an area in the fifth intercostal space in the mid-clavicular line. The right heart border could not be percussed because of fluid in the right chest. The left heart border was percussed 14 cm. from the midsternal line. A short diastolic thrill was palpable along the left sternal border. There was fullness in the third left intercostal space. A fairly harsh systolic and soft blowing diastolic murmur were heard at the apex, both becoming louder and harsher in the fourth left intercostal space parasternally, where a "machinery-like" character was assumed. At the very apex there was a suggestion of a short presystolic murmur with accentuation of the first sound. The second pulmonic sound was moderately accentuated. A short systolic and soft blowing diastolic murmur were present also at the aortic and pulmonic areas.

The abdomen was obese. The liver was palpable four fingerbreadths below the costal margin. The spleen was not felt, but the area of splenic dullness was increased. No abdominal masses were palpable. Rectal examination was normal. There was 4 plus pitting edema of the lower extremities. "Pistol-shot" sounds were audible over the femoral arteries. No clubbing was noted. Pin point punctate areas which did not blanch on pressure were noted under the nails of the second and third digits of the left hand. Neurologic examination was normal.

The clinical impression at this time was that the patient's symptoms were sudden in onset, and that she suffered from rheumatic heart disease with, possibly, superimposed bacterial endocarditis.

The possibility of a ruptured aortic leaflet was entertained, because of the loud and widespread diastolic murmur and the suddenness of the onset. However, the patient's seemingly fair condition did not really warrant the postulation of such a serious complication.

Laboratory Data.—

Urinalysis: Specific gravity 1.025, green color, albumin trace, sugar negative, acetone negative, bile and urobilinogen negative; sediment contained numerous bacteria and 12 leukocytes per high power field.

Homogram: Hemoblobin 70 per cent, R.B.C. 4.28 million, W.B.C. 5,300, polymorphonuclears 54, bend forms 1, lymphocytes 37, monocytes 8, 4 irritation cells, platelets adequate; 2 plus anisocytosis, slight poikilocytosis, 1 plus hypochromia, 1 plus polychromatophilia, and occasional targeting. Sedimentation rate 5 mm. per hour. Hematocrit 38 per cent.

Bacteriologic data: Culture of pharynx revealed Beta hemolytic streptococci, Alpha hemolytic streptococci, and nonhemolytic staphylococcus albus. Culture of pleural fluid was sterile. Blood culture revealed nonhemolytic staphylococcus albus, sensitive to 0.5 units per ml. of peni-

cillin, 1 μg. of tetracycline, 2 μg. of Aureomycin, 10 μg. of Terramycin and 20 units per milliliter of bacitracin. Two other blood cultures were sterile. Blood Kahn test was negative.

Electrocardiogram: ECG revealed low, isoelectric to slightly inverted T waves in all leads.

Roentgenograms: P-A view of chest revealed cardiac enlargement, prominence of left ventricular contour, and straightening of the left heart border. The right costophrenic sinus was blunted by pleural effusion (Fig. 1). Cardiac fluroscopy revealed a definite enlargement of the outflow tract of the right ventricle and of the left ventricle, increased pulmonary vascular pulsation, engorgement of secondary pulmonary vascular branches, and right pleural effusion. A plain film of the abdomen revealed no calcifications and normal bowel pattern.

Fig. 1.—X-ray. Posteroanterior view of the chest reveals cardiac enlargement, prominence of left ventricular contour, and straightening of the left heart border. The right costophrenic sinus is blunted by pleural effusion.

The patient was re-examined one week later, and the heart murmurs were found to be the same, but her condition seemed somewhat improved. However, because of the suddenness of the onset, the diastolic thrill at Erb's space, and the continuous murmur which was so widely spread, the previous diagnosis of rheumatic heart disease was abandoned in favor of that of a ruptured aneurysm of the right sinus of Valsalva into the pulmonary artery or into a right heart chamber.

Hospital Course.—Following admission, the patient was treated with bed rest, low salt diet, Mercuhydrin, digitalis (digitoxin 0.4 mg. initially and 0.2 mg. daily), aspirin (3 to 4 Gm. per day) and penicillin (600,000 units per day for several days). On the second hospital day right thoracentesis produced 20 c.c. of straw-colored fluid, culture of which was sterile. Temperature was recorded daily at levels below 99° F., tachycardia 100 to 108 per minute persisted. Pitting edema completely subsided and the patient became symptomatically more comfortable. Murmurs did not change in character or intensity. No embolic phenomona were noted. There was apparent increase in pallor of the conjunctivae and nail beds. In the second hospital week, the patient's general condition was considered much improved. She was ambulatory and relatively free of symptoms, although objectively slight edema of the ankles periodically recurred, tender hepatomegaly three fingerbreadths below the costal margin persisted, as did cervical vein distension, small right pleural effusion, and slight cough. On the seventeenth hospital day cardiac catheterization was performed uneventfully (Table I). An attempt at retrograde aortography by catheterization of the left brachial artery was unsuccessful. Following repair of the brachial artery, the radial and brachial pulsations were markedly diminished and the left upper extremity was cool, but without color change. Atropine and papaverine were given and a stellate ganglion

TABLE I. HEART CATHERIZATION DATA (DRS. DILLON AND WALLYN)

Name: M.D. Anesthetic: Local 1% Procaine Age: 19 yr. ____mo.
Date: 2–16–54 Premed.: None Height: 65″ cm.
Cath. No.: 54–020 Weight: 145 lb. Kg.
CCH No.: 54–6005 Surface area: 1.72m²
Normal O_2 cons. 180 c.c. per minute
RQ 9
Heart Rate: 110/minute BMR 18%

Blood Oxygen Content, Vol. %:

(3)	Inferior vena cava	7.08
(2)	Superior vena cava	5.65
(5)	Right atrium—upper	6.95
(4)	Right atrium—lower	8.18
(9)	Right ventricle—inflow	10.89
(8)	Right ventricle—mid	10.87
(6)	Pulmonary artery—right	10.51
(7)	Pulmonary artery—right	10.84
(1)	Right femoral artery	13.44
	Oxygen capacity RFA	15.18
	Oxygen saturation RFA	88.6%
	Hemoglobin (O_2 cap. + 1.36)	11.15 Gm. %
	Ear oximetry ( )	.....

Intravascular Pressures, S/D (mean):

	mm. Hg	*Normal*
Right atrium	(25)	(2–10)
Right atrium "a" wave	8	0–2½
Right ventricle	69/21–38 (41)	25/5
Pulmonary artery—right	61/31	25/10
Left subclavian artery	124/60 (100)	———
Right femoral artery	149/56 (88)	———
SVC	11 (22)	———
IVC	6 (24)	———

Spot Films: 1. Lower RA-IVC 2. _____ 3. _____ 4. _____

Calculated Blood Flows:

	Stroke c.c.
Systemic—2.52 L./min.; 1.46 L./min./M² (normal 3–3½)	23
Pulmonary—7.0 L./min.; 4.07 L./min./M² (normal 3–3½)	64
L-R shunt 4.5 2.61	41

Interpretation:

block was performed, resulting in a Horner's syndrome, and immediate subjective improvement but no change in the diminished pulsations. An attempt at brachial plexus block was attended by hemoptysis and sharp pain in the left third and fourth intercostal spaces anteriorly. On the following morning, radial pulse was improved but pain in the left arm had recurred. The left chest was hyperresonant and breath sounds were markedly diminished. The patient complained of pain over the left lower thorax posteriorly. X-ray showed minimal pneumothorax in the left upper lung field, with no displacement of the mediastinum.

Fig. 2.—Destruction of the noncoronary and right aortic cusps with perforation from the coronary sinuses toward the left ventricle.

On the nineteenth hospital day, the patient complained of considerable left anterior chest pain aggravated by inspiration and accompanied by a left pleural friction rub. Pulse was 120 per minute and electrocardiogram showed multifocal extrasystoles. On the twentieth day, severe chest pain persisted and signs of dullness and bronchophony were noted at the left lung base. A pleuropericardial friction rub was heard and expiratory grunt was noted. Thereafter dyspnea increased and respiratory rate rose to 40 per minute. Left thoracentesis produced 400 c.c. of straw-colored fluid which clotted almost immediately. Temperature rose to 100.8° F., the patient was given oxygen and penicillin; she became semistuporous, fine, dry, white crystalline material appeared on the face, and the patient expired on the twenty-second hospital day, after a total duration of illness of one month.

Right heart catheterization was accomplished under local procaine anesthesia via the left median basilic vein with a No. 7 catheter. Samples and pressures were taken from the cavae, RA, RV, PA. A large left-to-right shunt into the right heart is noted: probably the right ventricle with some regurgitation into the RA through the tricuspid valve. This regurgitation makes it impossible to state with certitude that the shunt is not into the RA with further mixing in the RV and PA. However, the RA pressure tracings show no unusual systolic or regurgitant (c) wave, as would be expected with an RA shunt.

The central venous pressure is equivalent to 325 mm. water with large "a" waves. The mean RA pressure is equivalent to the early diastolic RV pressure.

The RV pressure curve shows an early diastolic dip and late diastolic rise compatible with the decreased relaxability of myocardial dilation and failure or systemic communication. The diastolic plateau is 38/69 or 55 per cent of the systolic pressure.

The RV systolic and diastolic hypertension is transmitted to the PA.

The femoral pressure pulse wave (via direct needle puncture of RFA) revealed a tall peaked wave form with a large pulse pressure (149/56-93 mm. Hg) which is 62.5 per cent of the systolic pressure instead of the usual 33 per cent. The blood oxygen content revealed mild unsaturation.

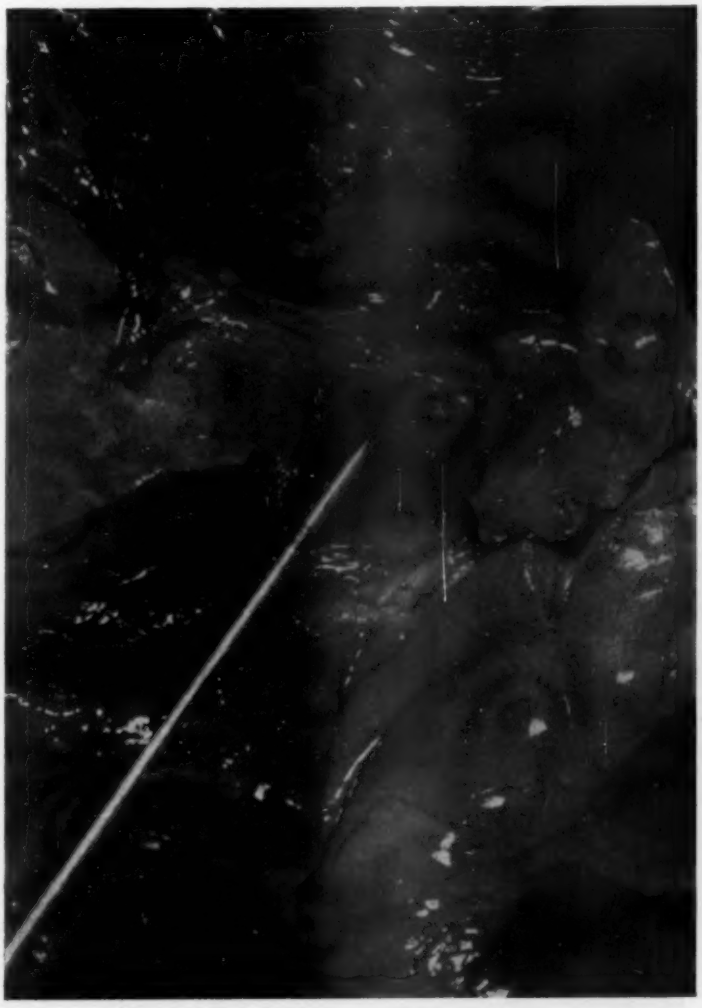

Fig. 3.—Aneurysm of right coronary sinus.

These findings are compatible with:

1. Ruptured sinus of Valsalva into the RV with RV failure and arterial unsaturation due to pulmonary congestion (or, a ruptured sinus into the PA with a previous IV septal defect).
2. An IV septal defect with aortic incompetence.
3. Patent ductus or aortic septal defect with pulmonary valvular incompetence.

The high incidence of IV septal defect in rupture of congenital sinuses of Valsalva (up to 40 per cent) makes definitive interpretation difficult.

The right ventricular pressure tracings showed a pattern reminiscent of a constricting or restricting lesion of the myocardium. The end diastolic pressure is over one-half of the systolic, and

is preceded by an early diastolic dip. Of course, correlation with the other data permitted no confusion. However, it is another example of the nonspecificity of the pattern. It is probably explained on the basis of diastolic overloading with maximal right ventricular dilatation.

Abstract of Autopsy.—(Dr. Hans Popper, Director of Dept. of Pathology, Cook County Hospital.) The body was that of a well-developed, well-nourished, 19-year-old girl, weighing 61 kg. and measuring 160 cm. in length. There was 1 plus pitting edema of the legs and 4 plus pitting edema of the sacral region.

The lungs were congested and edematous.

Fig. 4.—Rupture of the aneurysm of the right coronary sinus into the right ventricle. The probe demonstrates the communication between the aneurysm and the right ventricle.

The heart weighed 430 grams and was enlarged. The apex was formed by the left ventricle. The wall of the right ventricle measured 3 mm., and that of the left ventricle 14 mm. in thickness. T. O.—13.6 cm.; M.O.—10.2 cm.; P.O.—5.6 cm.; A.O.—7 cm. The leaflets of the tricuspid valve were thin and delicate. The posterior leaflet of the tricuspid valve contained a small hole measuring 2 mm. in diameter; this hole was situated near the attachment of the leaflet (Fig. 5). Immediately beneath this hole there was a round defect with a rather smooth edge in the ventricular septum. The cusps of the pulmonary valve were delicate. The mitral leaflets showed minimal thickening at the line of closure. The chordae tendineae were somewhat thickened.

The trabeculae and trabecular muscles of the left ventricle were flattened. The myocardium of the left ventricle failed to reveal any abnormality. The posterior and the right cusps of the aortic valve showed a large tonguelike friable red vegetation extending from the ventricular surface. The lower half of the posterior cusp, at its right side, had been destroyed by the vegetation, as had a small portion of the left border of the right cusp. Probes could be inserted into the left ventricle from the aorta through these defects (Fig. 2). There was a diffuse thickening of the right border of the posterior cusps. The right sinus of Valsalva showed a large aneurysmal pouching which ruptured into the right atrium (Fig. 3) and into the right ventricle (Fig. 4). The perforation into the ventricle was larger than that into the atrium. The coronary arteries were delicate and patent throughout.

The spleen weighed 115 grams, was firm in consistency, and showed a definite picture of chronic passive congestion. The liver was enlarged and congested.

The kidneys were congested.

Fig. 5.—Perforation of the tricuspid leaflet resulting in formation of a hole.

Microscopic Examinations.—

Heart: The microscopic examination of the aortic valve revealed vegetations, characterized by fibrinoid degeneration. Some areas were almost acellular, while other areas showed trapped cells in the fibrinoid mass. These cells were chiefly polymorphonuclear leukocytes. Other sections taken from the aortic cusp revealed recent verrucae associated with fibrinoid degeneration. The wall of the aneurysm proper showed marked fibrosis, with some superimposed fibrinoid degeneration. The sections taken from the myocardium showed evidence of acute myocarditis.

Summary and Pathologic Diagnosis.—This is the case of a congenital aneurysm of the right and posterior sinus of Valsalva which developed either from persisting trabecular spaces or rudimentary development of coronary vessels. Superimposed upon this aneurysm and superimposed upon a subclinical rheumatic valvulitis of the aortic valve, the patient developed an endocardiosis of the right and posterior aortic cusps which were deformed by the aneurysm. A bacterial infection of the endocardiosis led to the picture of a subacute bacterial endocarditis with rupture of the right posterior cusp. The endocardiosis involved the aneurysm itself, the wall of which

gave way and gradually ruptured into the right ventricle just below the tricuspid valve, and into the right atrium above the valve. The posterior tricuspid leaflet became involved and perforated, resulting in an acute incompetence of the tricuspid valve.

DISCUSSION

The correct diagnosis of congenital aneurysm of the sinuses of Valsalva cannot be made, unless there is rupture into one of the chambers of the heart, and the diagnosis must then depend upon the changes in the cardiodynamics. Boyd[8] pointed out that rupture commonly takes place into the pericardium, less commonly into the superior vena cava or pulmonary artery, and rarely into the chambers of the heart. In our case, the rupture occurred into both the right auricle and right ventricle. Death may ensue rapidly with rupture into the pericardium, but when rupture occurs into a heart cavity, or pulmonary artery, the patient may survive for days or weeks. Herrmann[9] cites a case that lasted for three years after the fistula developed. In our case the demise, no doubt, was greatly hastened by the unsuccessful attempt at retrograde aortography.

Needless to say, the size of the fistula determines to a large extent the clinical picture and the length of survival after the accident. Another factor that influences the prognosis adversely is the frequent presence of bacterial endocarditis in the sinus, or in one or more of the adjacent aortic leaflets, which is unrecognized. This occurred in our case. The presence of subacute bacterial endocarditis was debated between the various observers, and because of lack of any clinical evidence, it was decided in the negative. This was an error, for such patients should be given the benefit of the doubt and treated vigorously.

Clinically, the sudden onset of dyspnea with or without pain in the chest, the diastolic thrill in Erb's space, the widely spread humming, machine-like murmur, being most intense in the third to fourth left intercostal space; the wide pulse pressure, the signs of aortic insufficiency, and the expansile pulsation of the smaller branches of the pulmonary arteries fluoroscopically, constitute a syndrome of this shunt.

The cardiodynamics of this condition, as studied by catheterization of the heart, are interesting for several reasons. First, they point to the much graver prognosis of a significant acquired left-to-right shunt as compared with an equal or larger congenital shunt. This is partially explained by the fact that the acquired shunts are usually caused by a grave form of pathology, such as septal infarction or subacute bacterial endocarditis. However, even when the shunt is experimentally produced in animals, their course, too, is relatively rapid and fatal. This leads one to think that the important factor in the well-tolerated congenital shunts is the ability of the myocardium to accomodate and develop with this otherwise intolerable burden.

Secondly, the diagnostic problem is intricate and difficult to substantiate with absolute certitude. The essential points to be explained are: (1) a continuous systolic and diastolic murmur, (2) a wide pulse pressure, and (3) the left-to-right shunt noted at the ventricular level. The differential diagnosis includes: (1) patent ductus with pulmonary valvular insufficiency (to account for arterialization of the right ventricular samples), (2) patent ductus and an

interventricular septal defect, (3) coronary artery-right ventricular fistula, (4) aortic valvular insufficiency plus acquired or congenital interventricular septal defect, (5) ruptured aneurysm of a sinus of Valsalva into right ventricle (or pulmonary artery associated with an interventricular septal defect or pulmonary valvular insufficiency), and (6) acquired aortic-pulmonary artery fistula with pulmonary valvular insufficiency. It would seem that the only way to demonstrate a ruptured aneurysm of a sinus of Valsalva would be a retrograde aortogram which would: (1) outline the aneurysm, and (2) demonstrate regurgitation of the dye into the right ventricle without any in the left ventricle. This was attempted unsuccessfully. In retrospect, the perforation of an aortic valve would have made the test nondiagnostic. Also, it illustrates the danger of such aortograms when the patient's circulatory condition is so poor.

Thirdly, the mechanisms of failure are indeed so many and so malignant. They included: (1) myocarditis of subacute bacterial endocarditis, (2) aortic insufficiency, (3) pulmonary hypertension due mainly to the systolic shunt, (4) diastolic overloading due to the diastolic shunt, and (5) tricuspid regurgitation due to the jet-stream perforation of the tricuspid valve.

CONCLUSION

Aneurysm of the right sinus of Valsalva with rupture into the right atrium and into the right ventricle is reported.

Superimposed upon this aneurysm and upon a subclinical rheumatic valvulitis of the aortic valve, a subacute bacterial endocarditis was found, causing the rupture of the posterior aortic cusp, and of the aneurysm.

A correct antemortem diagnosis of rupture of the aneurysm was made based on the sudden onset, thrill, machinery-like murmur, and peripheral signs of aortic insufficiency.

Cardiac catheterization revealed a left-to-right shunt noted at the ventricular level, thus strengthening the clinical diagnosis, but not corroborating it.

A retrograde aortogram to outline the aneurysm and its rupture was attempted unsuccessfully.

It is strongly felt that since these patients frequently have a superimposed bacterial endocarditis, prompt and vigorous therapy with antibiotics should be carried out even in the doubtful cases.

SUMMARIO IN INTERLINGUA

Es reportate un caso de aneurysma del dextere sinus de Valsalva con ruptura a in atrio e ventriculo dextere.

Superimponite a site aneurysma e a un subclinic valvulitis rheumatic del valvula aortic, esseva trovate un subacute endocarditis bacterial le qual esseva le causa del ruptura del cuspide aortic posterior e del aneurysma.

Un correcte diagnose del ruptura del aneurysma esseva facite ante morte super le base del declaration subitanee del morbo, del fremito, del murmure mechanoide, e del signos peripheric de insufficientia aortic.

Catheterisation cardiac revelava un derivation sinistro-dextere, notate al nivello ventricular e reinfortiante (sin corroborar) le diagnose clinic.

Esseva tentate sin successo le registration de un aortogramma retrograde con le objectivo de determinar le contorno del aneurysma e su ruptura.

Nos opina con emphase que a causa del facto que patientes de iste typo ha frequentemente un superimponite endocarditis bacterial, un prompte e energic therapia antibiotic deberea esser initiate mesmo in casos dubitose.

We are indebted to Dr. Paul B. Szanto, Associate Director of the Department of Pathology, for his aid in preparing this report.

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Announcement

Preliminary Announcement of Course in Cardiology

On March 14 through 17, 1956, Dr. Samuel A. Levine, Clinical Professor of Medicine at Harvard Medical School, will present a course in Practical Bedside Cardiology at the Texas Medical Center, Houston, Texas. Dr. Levine will be the first lecturer for the J. J. and Una Truitt endowed Chair in Cardiology at The University of Texas Postgraduate School of Medicine. The course, co-sponsored by the Baylor University College of Medicine and the Houston Heart Association, will comprise three full days of clinical teaching by Dr. Levine. The registration fee of $35.00 entitles a registrant to attend all or any part of the course. Application should be made to The University of Texas Postgraduate School of Medicine, Texas Medical Center, Houston 25, Tex.

Addendum

It has been drawn to my attention that in the article "A Study of Electrocardiograms Recorded During Exercise Tests on Subjects in the Fasting State and after the Ingestion of a Heavy Meal," by Dr. C. H. Klakeg, Dr. R. D. Pruitt and myself, which appeared in the April, 1955, issue of the Journal, page 614, there was an omission of a certain article in the bibliography. This was published in the Revista Argentina de Cardiologia, 9:No. 6, 1943, entitled "El Electrocardiograma antes y despues del esfuerzo previa ingestion de alimentos," by Dr. Blas Moia and Dr. F. F. Battle.

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